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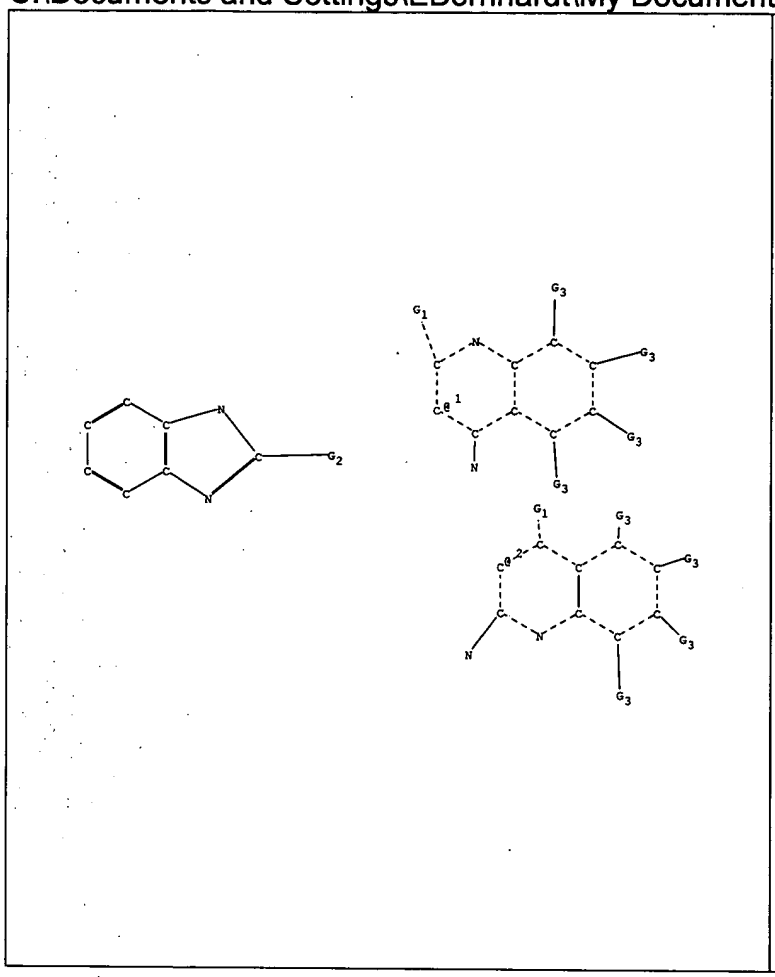

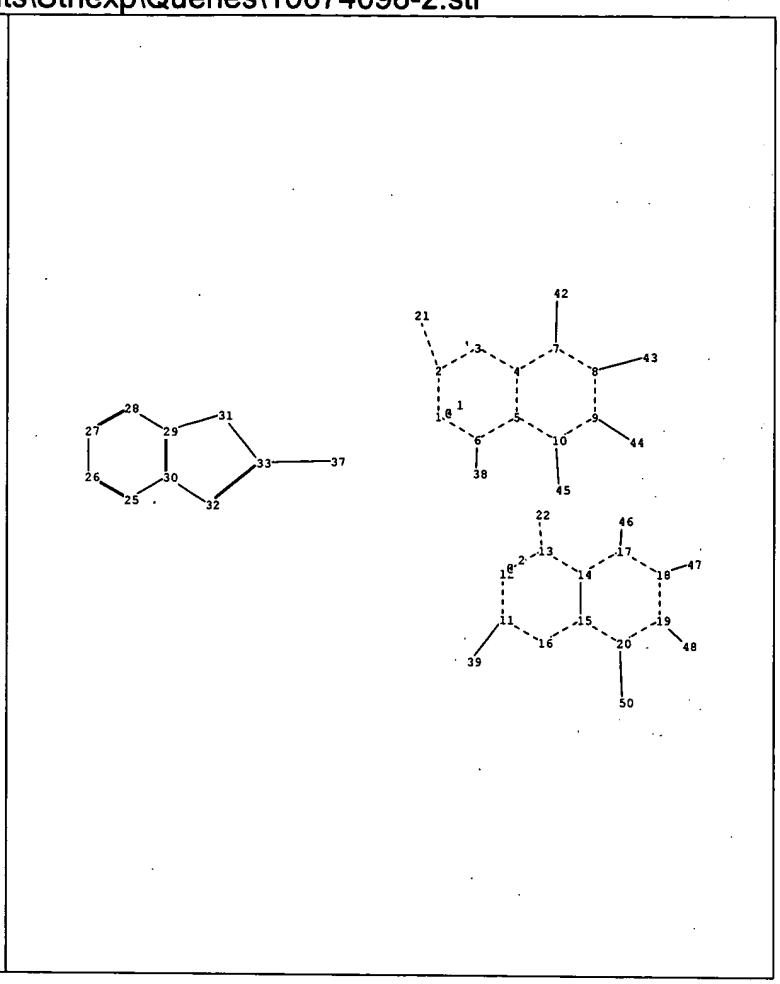

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ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 25 26 27 28 29 30 31 32 33
chain bonds :
2-21 6-38 7-42 8-43 9-44 10-45 11-39 13-22 17-46 18-47 19-48 20-50 33-37
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 14-17 15-16 15-20 17-18 18-19 19-20 25-26 25-30 26-27 27-28 28-29 29-30 29-31 30-32 31-33 32-33
exact/norm bonds :
1-2 1-6 2-3 2-21 3-4 4-5 4-7 5-6 5-10 6-38 7-8 7-42 8-9 8-43 9-10 9-44 10-45 11-12 11-16 11-39 12-13 13-14 13-22 14-15 14-17 15-16 15-20 17-18 17-46 18-19 18-47 19-20 19-48 20-50 29-31 30-32 31-33 32-33 33-37
normalized bonds :
25-26 25-30 26-27 27-28 28-29 29-30
isolated ring systems :
containing 1 : 11 : 25 :

G1:O,S

G2:[*1],[*2]

G3:H,CH3

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS 22:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 37:CLASS 38:CLASS 39:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 50:CLASS

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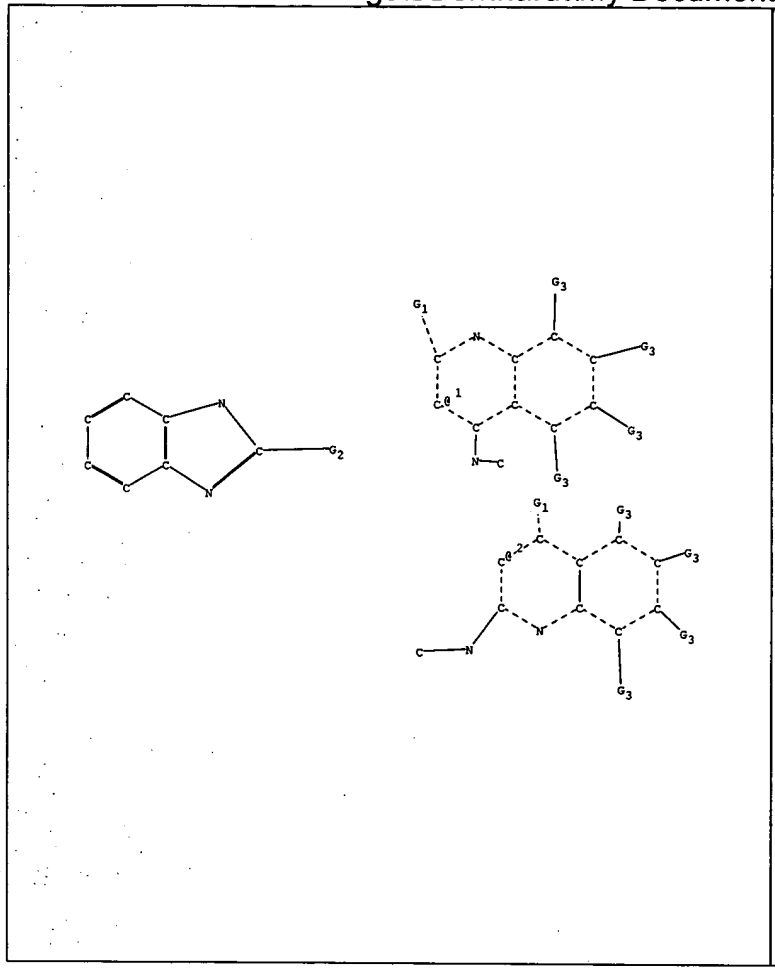

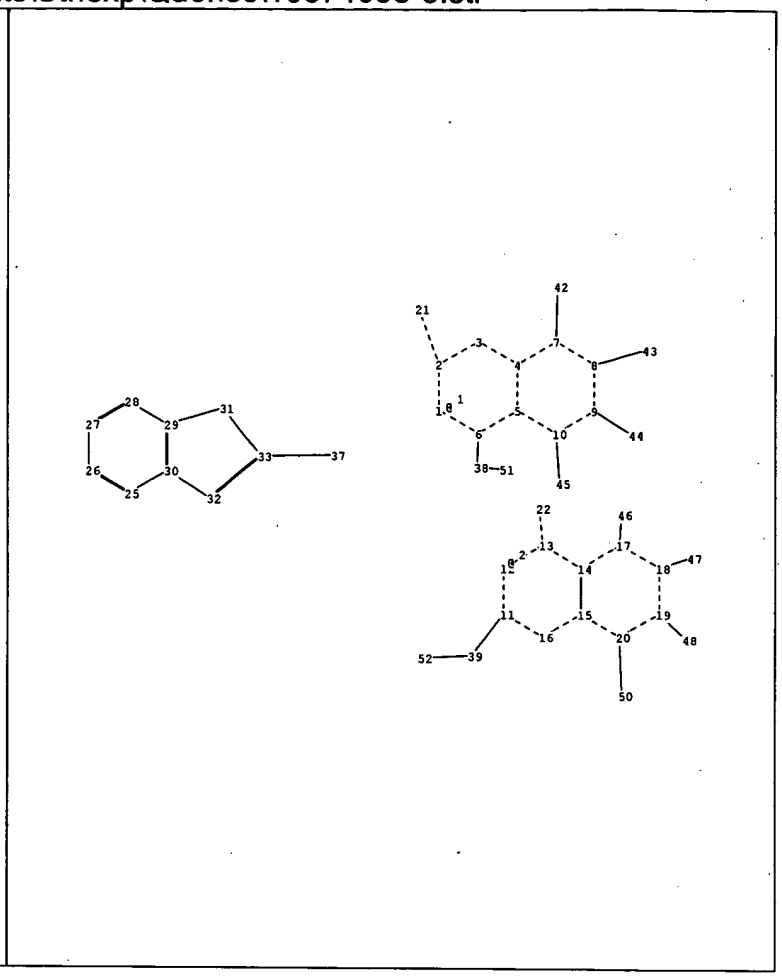

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ring nodes :
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chain bonds :
2-21 6-38 7-42 8-43 9-44 10-45 11-39 13-22 17-46 18-47 19-48 20-50 33-37 38-51 39-52
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 14-17 15-16 15-20 17-18 18-19 19-20 25-26 25-30 26-27 27-28 28-29 29-30 29-31 30-32 31-33 32-33
exact/norm bonds :
1-2 1-6 2-3 2-21 3-4 4-5 4-7 5-6 5-10 6-38 7-8 7-42 8-9 8-43 9-10 9-44 10-45 11-12 11-16 11-39 12-13 13-14 13-22 14-15 14-17 15-16 15-20 17-18 17-46 18-19 18-47 19-20 19-48 20-50 29-31 30-32 31-33 32-33 33-37 38-51 39-52
normalized bonds :
25-26 25-30 26-27 27-28 28-29 29-30
isolated ring systems :
containing 1 : 11 : 25 :

G1:O,S

G2:[*1],[*2]

G3:H,CH3

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS 22:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 37:CLASS 38:CLASS 39:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 50:CLASS 51:CLASS 52:CLASS

10/674098-subset search results

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptau122ebb

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 18:07:27 ON 08 NOV 2006
FILE 'CAPLUS' ENTERED AT 18:07:27 ON 08 NOV 2006
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	113.62	290.43

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.75	-12.75

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	113.62	290.43

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.75	-12.75

FILE 'REGISTRY' ENTERED AT 18:07:38 ON 08 NOV 2006
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DICTIONARY FILE UPDATES: 7 NOV 2006 HIGHEST RN 912617-52-8

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predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

10/674098-subset search results

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L4             12 S L3
L5            256 S L3 SSS FULL
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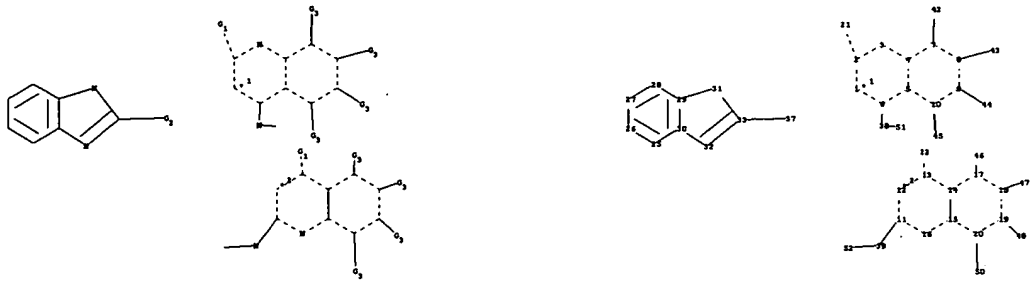

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21  22  37  38  39  42  43  44  45  46  47  48  50  51  52
ring nodes :
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28  29  30  31  32  33
chain bonds :
2-21  6-38  7-42  8-43  9-44  10-45  11-39  13-22  17-46  18-47  19-48  20-50
33-37  38-51  39-52
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10/674098-subset search results

ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 14-17 15-16 15-20 17-18 18-19 19-20 25-26 25-30 26-27 27-28 28-29
29-30 29-31 30-32 31-33 32-33
exact/norm bonds :
1-2 1-6 2-3 2-21 3-4 4-5 4-7 5-6 5-10 6-38 7-8 7-42 8-9 8-43 9-10
9-44 10-45 11-12 11-16 11-39 12-13 13-14 13-22 14-15 14-17 15-16 15-20
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38-51 39-52
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isolated ring systems :
containing 1 : 11 : 25 :

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G2:[*1],[*2]

G3:H,CH3

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1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
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100.0% PROCESSED 77 ITERATIONS 40 ANSWERS
SEARCH TIME: 00.00.01

L8 40 SEA SUB=L5 SSS FUL L7

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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

FULL ESTIMATED COST 40.72 331.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION

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FILE LAST UPDATED: 7 Nov 2006 (20061107/ED)

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L9 10 L8

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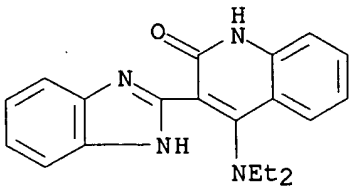
L9 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:453877 CAPLUS
DN 145:124498
TI 4-(Aminoalkylamino)-3-benzimidazole-quinolinones as potent CHK-1 inhibitors
AU Ni, Zhi-Jie; Barsanti, Paul; Brammeier, Nathan; Diebes, Anthony; Poon, Daniel J.; Ng, Simon; Pecchi, Sabina; Pfister, Keith; Renhowe, Paul A.; Ramurthy, Savithri; Wagman, Allan S.; Bussiere, Dirksen E.; Le, Vincent; Zhou, Yasheen; Jansen, Johanna M.; Ma, Sylvia; Gesner, Thomas G.
CS Chiron Corporation, Emeryville, CA, 94608, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(12), 3121-3124
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 145:124498
IT 668423-51-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 4-(aminoalkylamino)-3-benzimidazolyl-2-quinolinones as potent CHK-1 inhibitors with synergistic effect with a DNA-damaging agent (camptothecin))
RN 668423-51-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(diethylamino)- (9CI) (CA INDEX NAME)

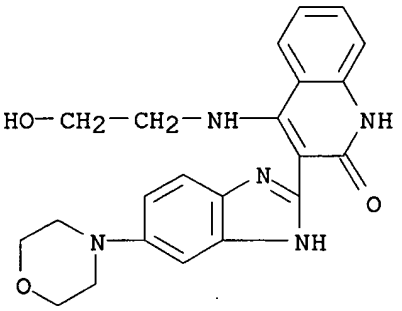


RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1242789 CAPLUS
DN 143:477969
TI Preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma
IN Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla C.; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Wiesmann, Marion; Zhu, Shuguang
PA Chiron Corporation, USA
SO U.S. Pat. Appl. Publ., 239 pp., Cont.-in-part of U.S. Ser. No. 644,055.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005261307	A1	20051124	US 2004-983174	20041105
	US 2004092535	A1	20040513	US 2003-644055	20030819
	CN 1692112	A	20051102	CN 2003-824565	20030819
	US 2005203101	A1	20050915	US 2004-839793	20040505
PRAI	US 2002-405729P	P	20020823		
	US 2002-426107P	P	20021113		
	US 2002-426226P	P	20021113		
	US 2002-426282P	P	20021113		
	US 2002-428210P	P	20021121		
	US 2003-460327P	P	20030403		
	US 2003-460328P	P	20030403		
	US 2003-460493P	P	20030403		
	US 2003-478916P	P	20030616		
	US 2003-484048P	P	20030701		
	US 2003-644055	A2	20030819		
	US 2003-517915P	P	20031107		
	US 2003-526425P	P	20031202		
	US 2003-526426P	P	20031202		
	US 2004-546017P	P	20040219		

OS MARPAT 143:477969
IT 405168-26-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma)
RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



L9 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1223876 CAPLUS
DN 143:477966
TI Preparation of benzimidazole quinolinones for inhibiting a checkpoint kinase 1 and their use in combination therapy for cancer
IN Gesner, Thomas G.; Barsanti, Paul A.; Harrison, Stephen D.; Ni, Zhi-Jie; Brammeier, Nathan M.; Zhou, Yasheen; Le, Vincent P.
PA Chiron Corporation, USA
SO U.S. Pat. Appl. Publ., 249 pp., Cont.-in-part of U.S. Ser. No. 644,055.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005256157	A1	20051117	US 2005-41191	20050121
	US 2004092535	A1	20040513	US 2003-644055	20030819
	CN 1692112	A	20051102	CN 2003-824565	20030819
	US 2005203101	A1	20050915	US 2004-839793	20040505
PRAI	US 2002-405729P	P	20020823		
	US 2002-426107P	P	20021113		
	US 2002-426226P	P	20021113		
	US 2002-426282P	P	20021113		
	US 2002-428210P	P	20021121		
	US 2003-460327P	P	20030403		
	US 2003-460328P	P	20030403		
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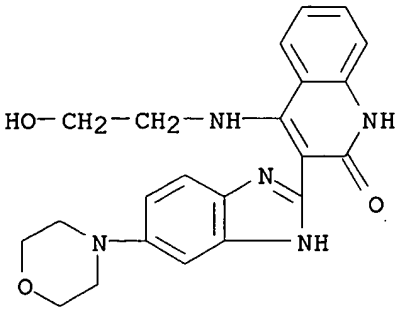
	US 2004-538984P	P	20040123		

OS MARPAT 143:477966
IT 405168-26-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones for inhibiting a checkpoint kinase 1 and their use in combination therapy for cancer)
RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



L9 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:976928 CAPLUS
DN 143:279443
TI 4-Amino-3-(benzimidazol-2-yl)quinolin-2-one derivatives for the modulation of inflammatory and metastatic processes
IN Lee, Sang H.; Heise, Carla C.
PA Chiron Corporation, USA
SO PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005082340	A2	20050909	WO 2005-US5316	20050218
	WO 2005082340	A3	20060504		
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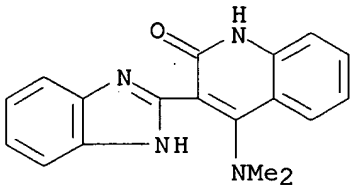
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005216904	A1	20050909	AU 2005-216904	20050218
	CA 2556872	AA	20050909	CA 2005-2556872	20050218
	US 2005239825	A1	20051027	US 2005-61386	20050218
PRAI	US 2004-546395P	P	20040220		
	US 2004-547103P	P	20040223		
	US 2004-554771P	P	20040319		
	WO 2005-US5316	W	20050218		

OS MARPAT 143:279443
IT 405170-04-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzimidazolyl aminoquinolinone derivs. for modulation of inflammatory and metastatic processes)
RN 405170-04-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA INDEX NAME)



L9 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:451351 CAPLUS
DN 143:7710
TI Preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma
IN Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla C.; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Wiesmann, Marion; Zhu, Shuguang
PA Chiron Corporation, USA
SO PCT Int. Appl., 567 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

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PI	WO 2005047244	A2	20050526	WO 2004-US36956	20041105
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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OS MARPAT 143:7710
IT 405168-26-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
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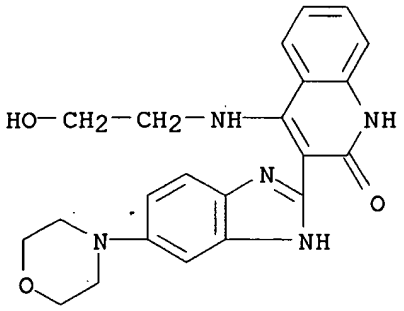
RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



L9 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:451118 CAPLUS
DN 143:7709
TI Preparation of benzimidazole quinolinones and lactate salts thereof for inhibiting vascular endothelial growth factor receptor tyrosine kinase
IN Cai, Shaopei; Chou, Joyce; Harwood, Eric; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Zhu, Shuguang
PA Chiron Corporation, USA
SO PCT Int. Appl., 215 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005046589	A2	20050526	WO 2004-US36941	20041105
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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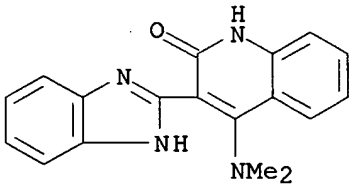
	CA 2544492	AA	20050526	CA 2004-2544492	20041105
	US 2005137399	A1	20050623	US 2004-982757	20041105
	US 2005209247	A1	20050922	US 2004-982543	20041105
	EP 1699421	A2	20060913	EP 2004-816941	20041105
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
PRAI	US 2003-517915P	P	20031107		
	US 2003-526425P	P	20031202		
	US 2003-526426P	P	20031202		
	US 2004-546017P	P	20040219		

WO 2004-US36941 W 20041105
OS CASREACT 143:7709; MARPAT 143:7709
IT 405170-04-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones and lactate salts thereof for inhibiting vascular endothelial growth factor receptor tyrosine kinase)
RN 405170-04-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA INDEX NAME)



L9 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:310953 CAPLUS
DN 140:321363
TI Preparation of [(piperazinyl)benzimidazolyl]quinolinones and analogs as tyrosine kinase inhibitors for treatment of cancer
IN Velaparthi, Upender; Wittman, Mark D.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004030620	A2	20040415	WO 2003-US30669	20030929
	WO 2004030620	A3	20040610		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003275282	A1	20040423	AU 2003-275282	20030929
	US 2004092514	A1	20040513	US 2003-674098	20030929
	EP 1545529	A2	20050629	EP 2003-759558	20030929
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-415066P	P	20020930		
	WO 2003-US30669	W	20030929		

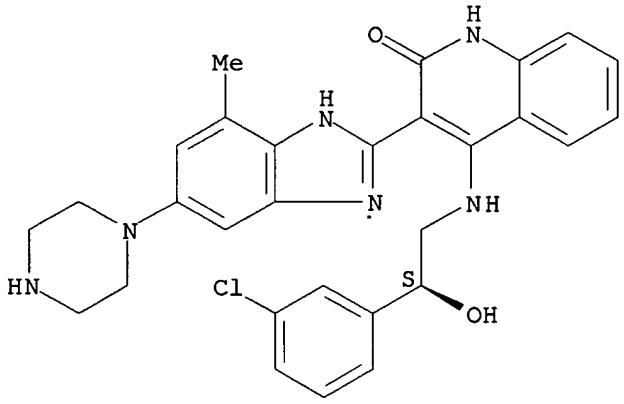
OS MARPAT 140:321363
IT 677341-90-1P, 4-[[(S)-2-(3-Chlorophenyl)-2-hydroxyethyl]amino]-3-

[4-methyl-6-(piperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(tyrosine kinase inhibitor; preparation of [(piperazinyl)benzimidazolyl]quinolinones and analogs as tyrosine kinase inhibitors for treatment of cancer)

RN 677341-90-1 CAPLUS

CN 2(1H)-Quinolinone, 4-[[(2S)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-3-[4-methyl-6-(1-piperazinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:182836 CAPLUS

DN 140:235711

TI Preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase

IN Barsanti, Paul A.; Bussiere, Dirksen; Harrison, Stephen D.; Heise, Carla C.; Jansen, Johanna M.; Jazan, Elisa; Machajewski, Timothy D.; Mcbride, Christopher; McCrea, William R.; Ng, Simon; Ni, Zhi-Jie; Pecchi, Sabina; Pfister, Keith; Ramurthy, Savithri; Renhowe, Paul A.; Shafer, Cynthia M.; Silver, Joel B.; Wagman, Allan; Weismann, Marion

PA Chiron Corporation, USA

SO PCT Int. Appl., 570 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004018419	A2	20040304	WO 2003-US25990	20030819
	WO 2004018419	A3	20040603		
	WO 2004018419	B1	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

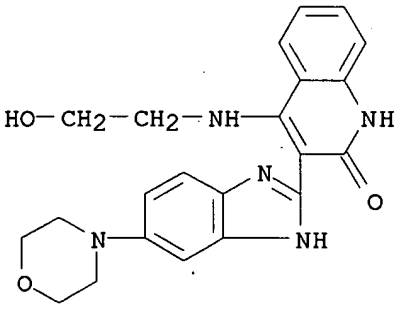
	CA 2496164	AA	20040304	CA 2003-2496164	20030819
	AU 2003288899	A1	20040311	AU 2003-288899	20030819
	EP 1539754	A2	20050615	EP 2003-781286	20030819
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003013743	A	20050705	BR 2003-13743	20030819
	CN 1692112	A	20051102	CN 2003-824565	20030819
	JP 2006503919	T2	20060202	JP 2005-501762	20030819
PRAI	US 2002-405729P	P	20020823		
	US 2002-426107P	P	20021113		
	US 2002-426226P	P	20021113		
	US 2002-426282P	P	20021113		
	US 2002-428210P	P	20021121		
	US 2003-460327P	P	20030403		
	US 2003-460328P	P	20030403		
	US 2003-460493P	P	20030403		
	US 2003-478916P	P	20030616		
	US 2003-484048P	P	20030701		
	WO 2003-US25990	W	20030819		

OS MARPAT 140:235711

IT 405168-26-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase)

RN 405168-26-5 CAPLUS

CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



L9 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:98039 CAPLUS

DN 138:153534

TI Preparation of benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents

IN Renhowe, Paul A.; Pecchi, Sabina; Machajewski, Timothy D.; Shafer, Cynthia M.; Taylor, Clarke; McCrea, William R.; McBride, Christopher; Jazan, Elisa

PA Chiron Corporation, USA

SO U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U.S. Pat. Appl. 2002

107,392.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003028018	A1	20030206	US 2002-116117	20020405
	US 2002107392	A1	20020808	US 2001-951265	20010911
	US 6605617	B2	20030812		
	EP 1650203	A1	20060426	EP 2005-17665	20010911
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	US 2003158224	A1	20030821	US 2002-284017	20021030
	US 6774237	B2	20040810		
	US 2004006101	A1	20040108	US 2003-387355	20030312
	US 6762194	B2	20040713		
	CA 2481055	AA	20031023	CA 2003-2481055	20030404
	WO 2003087095	A1	20031023	WO 2003-US10463	20030404
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003226275	A1	20031027	AU 2003-226275	20030404
	EP 1497287	A1	20050119	EP 2003-746614	20030404
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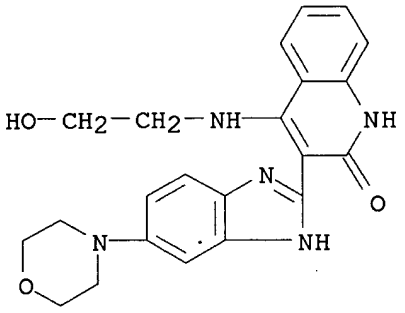
	BR 2003008996	A	20050222	BR 2003-8996	20030404
	CN 1659165	A	20050824	CN 2003-812909	20030404
	JP 2005527587	T2	20050915	JP 2003-584051	20030404
	US 2004097545	A1	20040520	US 2003-613411	20030703
	US 6800760	B2	20041005		
	US 2005054672	A1	20050310	US 2004-886950	20040708
	NO 2004004776	A	20041207	NO 2004-4776	20041103
	US 2005209456	A1	20050922	US 2005-92137	20050329
PRAI	US 2000-232159P	P	20000911		
	US 2001-951265	A2	20010911		
	EP 2001-973722	A3	20010911		
	US 2002-116117	A	20020405		
	US 2002-284017	A1	20021030		
	WO 2003-US10463	W	20030404		
	US 2004-886950	A1	20040708		

OS MARPAT 138:153534
IT 405168-26-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)
RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-

benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



L9 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:220574 CAPLUS
DN 136:263158
TI Benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents
IN Renhowe, Paul; Pecchi, Sabina; Machajewski, Tim; Shafer, Cynthia; Taylor, Clarke; McCrea, Bill; McBride, Chris; Jazan, Elisa; Wernette-Hammond, Mary-Ellen; Harris, Alex
PA Chiron Corporation, USA
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002022598	A1	20020321	WO 2001-US42131	20010911
	WO 2002022598	C1	20021121		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2421120	AA	20020321	CA 2001-2421120	20010911
	AU 2001093275	A5	20020326	AU 2001-93275	20010911
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	EP 1317442	B1	20051116		
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	NZ 524717	A	20040924	NZ 2001-524717	20010911
	AT 309996	E	20051215	AT 2001-973722	20010911
	ES 2250480	T3	20060416	ES 2001-1973722	20010911
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	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
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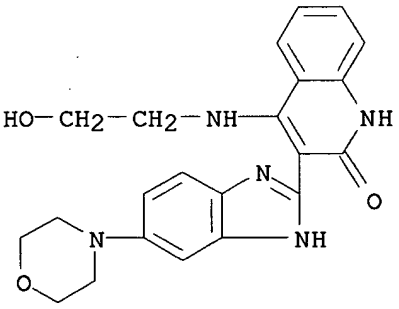
	NO 2003001097	A	20030325	NO 2003-1097	20030310
	US 2004006101	A1	20040108	US 2003-387355	20030312
	US 6762194	B2	20040713		
	BG 107709	A	20040130	BG 2003-107709	20030408
	HK 1053644	A1	20060504	HK 2003-104217	20030612
	US 2005054672	A1	20050310	US 2004-886950	20040708
	US 2005209456	A1	20050922	US 2005-92137	20050329
	AU 2005202068	A1	20050602	AU 2005-202068	20050513
PRAI	US 2000-232159P	P	20000911		
	AU 2001-293275	A3	20010911		
	EP 2001-973722	A3	20010911		
	US 2001-951265	A1	20010911		
	WO 2001-US42131	W	20010911		
	US 2002-284017	A1	20021030		
	US 2004-886950	A1	20040708		

OS MARPAT 136:263158

IT 405168-26-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

RN 405168-26-5 CAPLUS

CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L9 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:1242789 CAPLUS

DN 143:477969

TI Preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma

IN Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla C.; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Wiesmann, Marion; Zhu, Shuguang

PA Chiron Corporation, USA

SO U.S. Pat. Appl. Publ., 239 pp., Cont.-in-part of U.S. Ser. No. 644,055.

CODEN: USXXCO
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005261307	A1	20051124	US 2004-983174	20041105
	US 2004092535	A1	20040513	US 2003-644055	20030819
	CN 1692112	A	20051102	CN 2003-824565	20030819
	US 2005203101	A1	20050915	US 2004-839793	20040505
PRAI	US 2002-405729P	P	20020823		
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	US 2002-426282P	P	20021113		
	US 2002-428210P	P	20021121		
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OS MARPAT 143:477969
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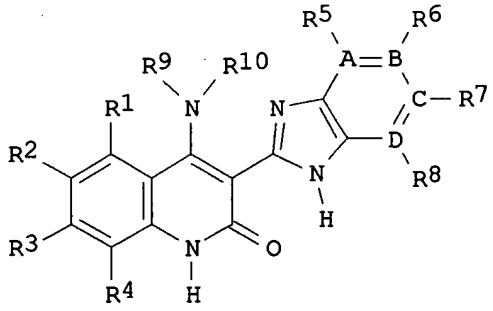

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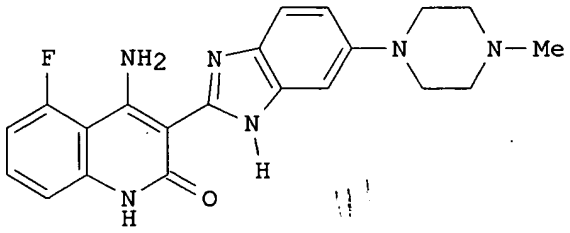


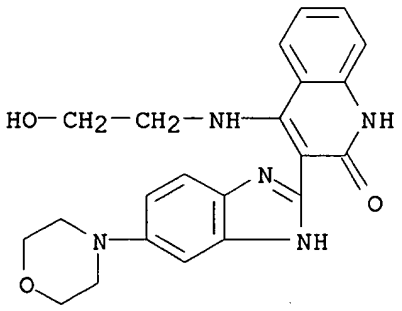
II

AB The title compds. I [A, B, C, and D = C, N; R1-R3 = H, halo, CN, NO2, etc.; R4 = H, alkyl; R5-R8 = H, halo, CN, NO2, etc.; R9 = H,

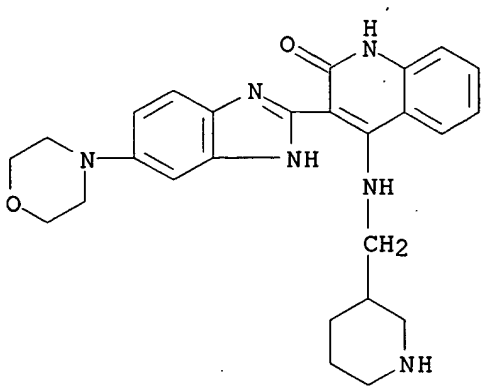
(un)substituted alkyl, aryl, etc.; R10 = H], useful for inhibiting fibroblast growth factor receptor 3 or treating a biol. condition mediated by fibroblast growth factor receptor 3, were prepared E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one (II), starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM. The mentioned above compound II was tested in various tests and showed significant antiproliferative activity. II inhibited FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

IT 405168-26-5P 405168-29-8P 405168-30-1P
405168-31-2P 405168-32-3P 405168-38-9P
405168-39-0P 405168-40-3P 405168-41-4P
405168-47-0P 405170-04-9P 405170-84-5P
405170-85-6P 405170-86-7P 405170-87-8P
668422-85-3P 668423-39-0P 668423-40-3P
668423-43-6P 668423-44-7P 668423-47-0P
668423-51-6P 668423-52-7P 668423-81-2P
668424-44-0P 668424-49-5P 668424-52-0P
668429-04-7P 668429-07-0P 668429-10-5P
668429-13-8P 668429-15-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma)

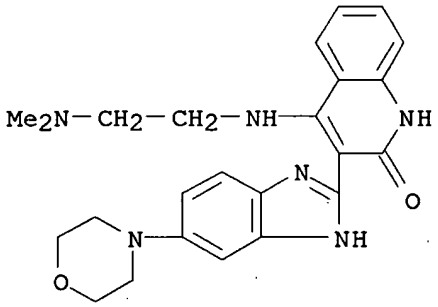
RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



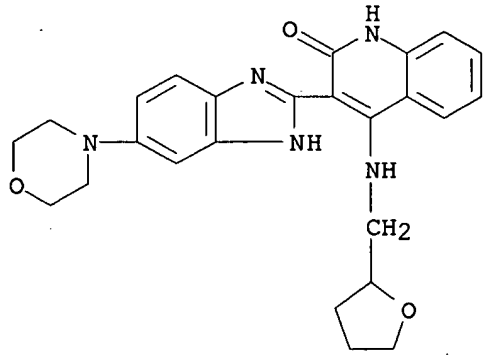
RN 405168-29-8 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



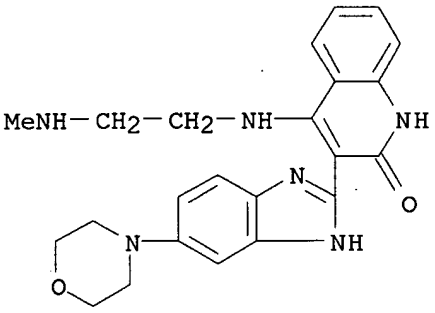
RN 405168-30-1 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(dimethylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



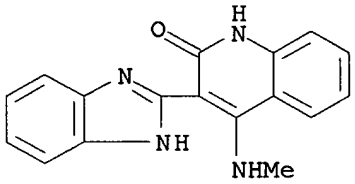
RN 405168-31-2 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



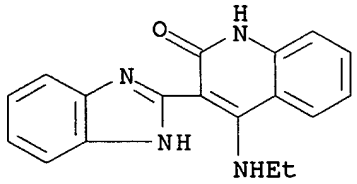
RN 405168-32-3 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(methylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



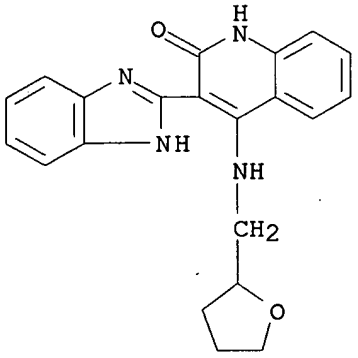
RN 405168-38-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(methylamino)- (9CI) (CA INDEX NAME)



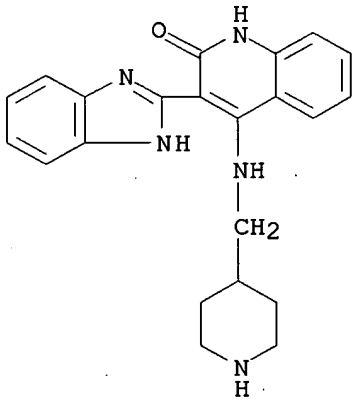
RN 405168-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(ethylamino)- (9CI) (CA INDEX NAME)



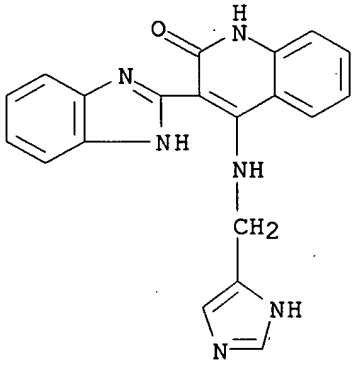
RN 405168-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 405168-41-4 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

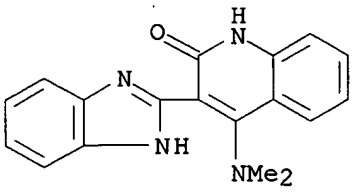


RN 405168-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-4-ylmethyl)amino]- (9CI) (CA INDEX NAME)

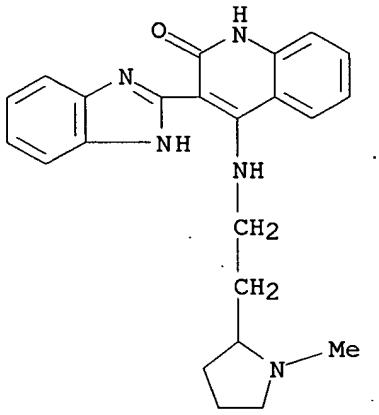


RN 405170-04-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA

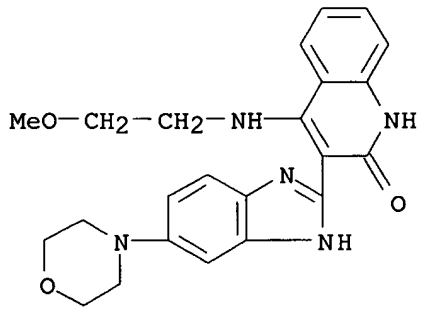
INDEX NAME)



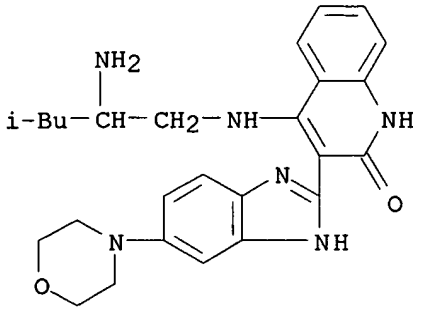
RN 405170-84-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



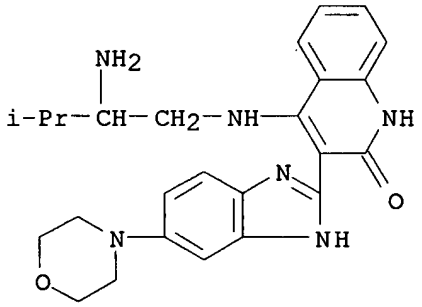
RN 405170-85-6 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



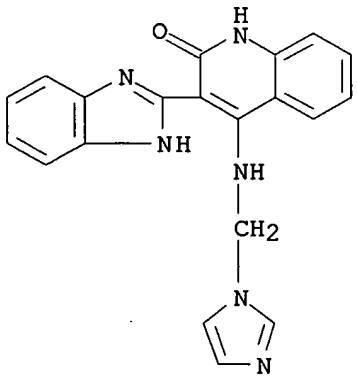
RN 405170-86-7 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-4-methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



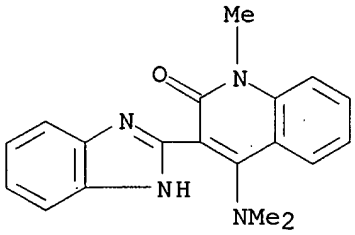
RN 405170-87-8 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



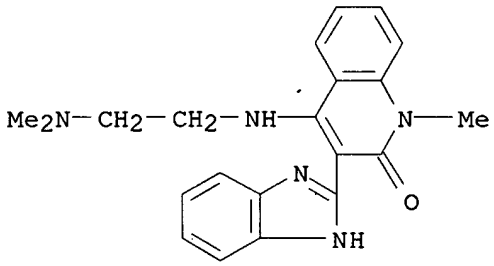
RN 668422-85-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-1-ylmethyl)amino]- (9CI) (CA INDEX NAME)



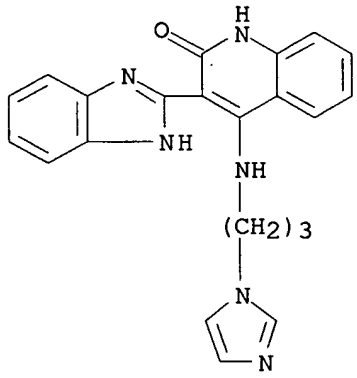
RN 668423-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)-1-methyl- (9CI) (CA INDEX NAME)



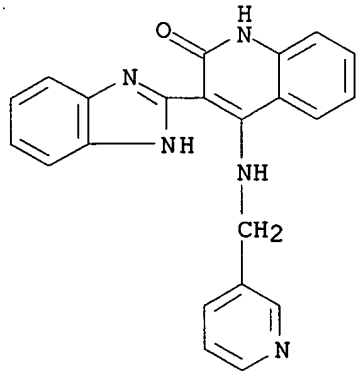
RN 668423-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



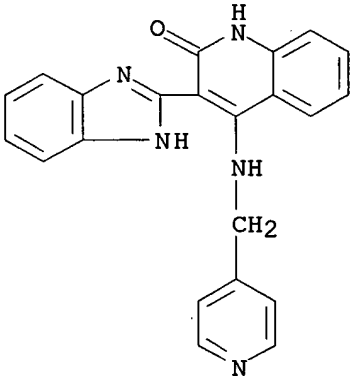
RN 668423-43-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[3-(1H-imidazol-1-yl)propyl]amino]- (9CI) (CA INDEX NAME)



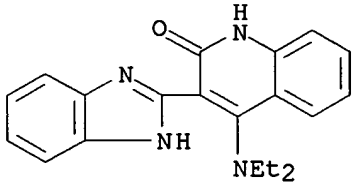
RN 668423-44-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



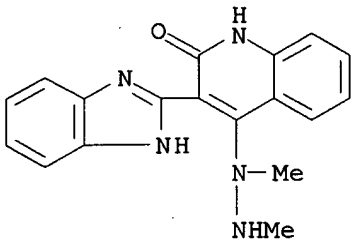
RN 668423-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



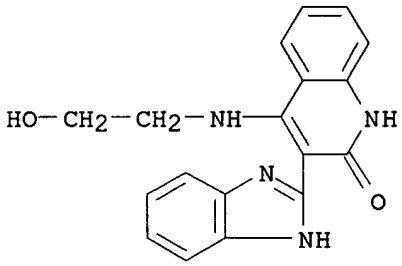
RN 668423-51-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(diethylamino)- (9CI) (CA INDEX NAME)



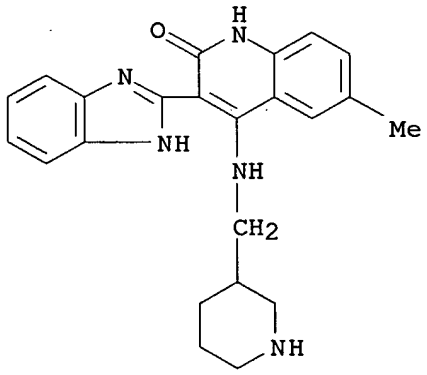
RN 668423-52-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(1,2-dimethylhydrazino)- (9CI) (CA INDEX NAME)



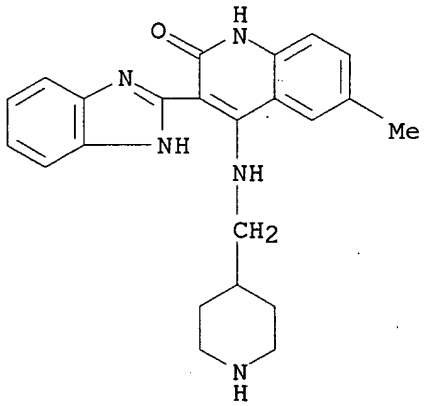
RN 668423-81-2 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(2-hydroxyethyl)amino]- (9CI) (CA INDEX NAME)



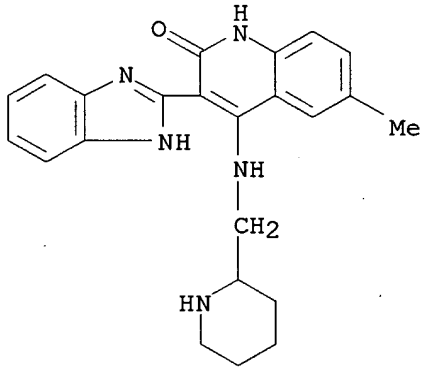
RN 668424-44-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



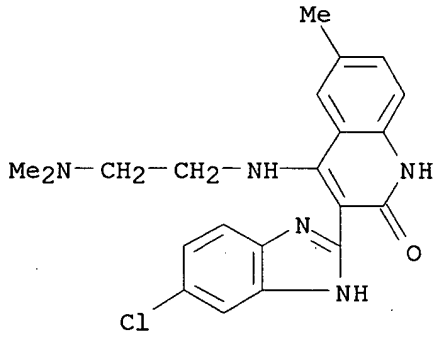
RN 668424-49-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 668424-52-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

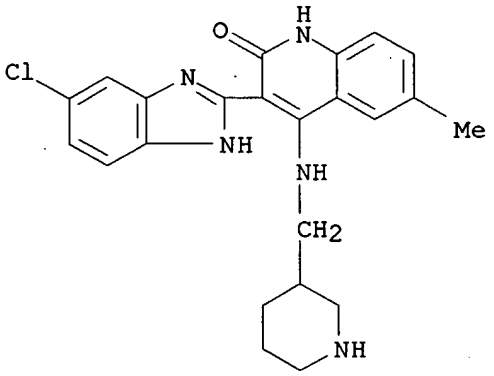


RN 668429-04-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-6-methyl- (9CI) (CA INDEX NAME)

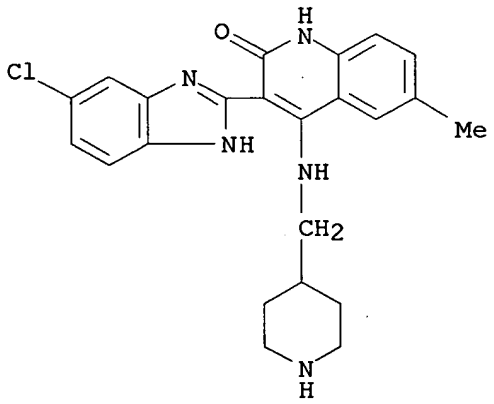


RN 668429-07-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(3-

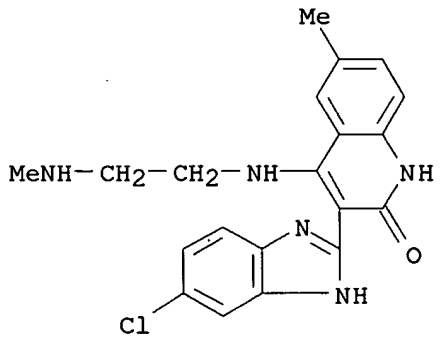
piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



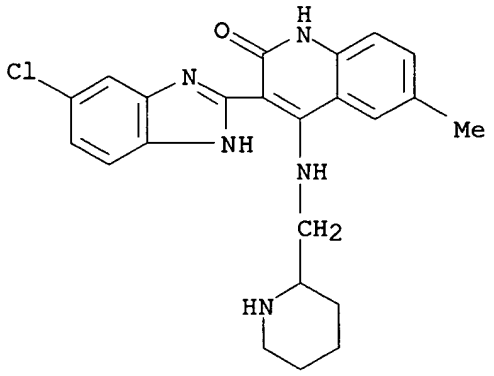
RN 668429-10-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



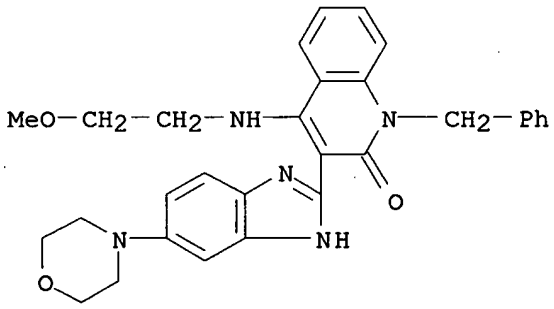
RN 668429-13-8 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[[2-(methylamino)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 668429-15-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



IT 405171-07-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma)
RN 405171-07-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1223876 CAPLUS
DN 143:477966
TI Preparation of benzimidazole quinolinones for inhibiting a checkpoint kinase 1 and their use in combination therapy for cancer
IN Gesner, Thomas G.; Barsanti, Paul A.; Harrison, Stephen D.; Ni, Zhi-Jie; Brammeier, Nathan M.; Zhou, Yasheen; Le, Vincent P.
PA Chiron Corporation, USA
SO U.S. Pat. Appl. Publ., 249 pp., Cont.-in-part of U.S. Ser. No. 644,055.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 7

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	US 2005256157	A1	20051117	US 2005-41191	20050121
	US 2004092535	A1	20040513	US 2003-644055	20030819
	CN 1692112	A	20051102	CN 2003-824565	20030819
	US 2005203101	A1	20050915	US 2004-839793	20040505
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	US 2002-426226P	P	20021113		
	US 2002-426282P	P	20021113		
	US 2002-428210P	P	20021121		
	US 2003-460327P	P	20030403		
	US 2003-460328P	P	20030403		
	US 2003-460493P	P	20030403		
	US 2003-478916P	P	20030616		
	US 2003-484048P	P	20030701		
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	US 2004-538984P	P	20040123		
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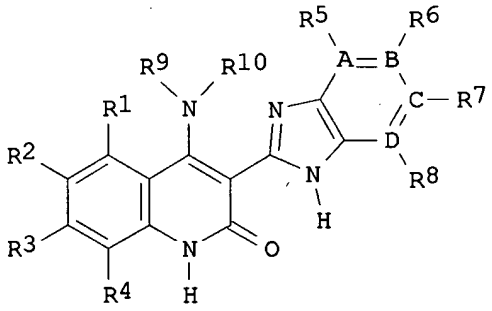
GI					



I

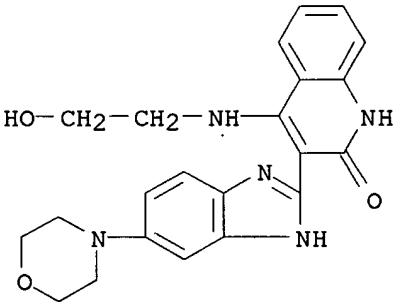
AB The title compds. [I; A, B, C, D = C, N; R1 = H, halo, CN, NO2, etc.; R2, R3 = H, halo, NO2, CN, etc.; R4 = H, (un)substituted alkyl; R5, R8 = H, (un)substituted alkyl, alkenyl, heterocyclyl; or R5 may be absent if A = N; or R8 may be absent if D = N; R6, R7 = H, halo, NO2, CN, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or R9 and R10 join together to form one or more rings, each having 5-7 members], useful for inhibiting checkpoint kinase 1, inducing cell cycle progression, and increasing apoptosis in cells, were prepared E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The compds. I were tested against various kinases. Two of the prepared compds. I, 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benimidazol-2-yl)-6-chloroquinolin-2-(1H)-one and 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one, were found to be potent inhibitors of CHK1 with IC50 of 0.32 nM and 0.63 nM, resp. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3,

c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM. The compds. I may be used to prepare pharmaceutical compns. and may be used in conjunction with DNA damaging agents.

IT 405168-26-5P 405168-29-8P 405168-30-1P
405168-31-2P 405168-32-3P 405168-38-9P
405168-39-0P 405168-40-3P 405168-41-4P
405168-47-0P 405170-04-9P 405170-84-5P
405170-85-6P 405170-86-7P 405170-87-8P
668422-85-3P 668423-39-0P 668423-40-3P
668423-43-6P 668423-44-7P 668423-47-0P
668423-51-6P 668423-52-7P 668423-81-2P
668424-44-0P 668424-49-5P 668424-52-0P
668429-04-7P 668429-07-0P 668429-10-5P
668429-13-8P 668429-15-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones for inhibiting a checkpoint kinase 1 and their use in combination therapy for cancer)

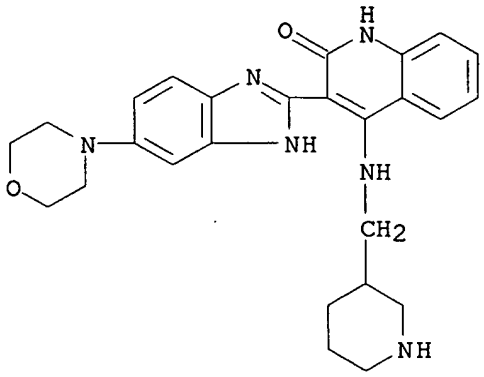
RN 405168-26-5 CAPLUS

CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

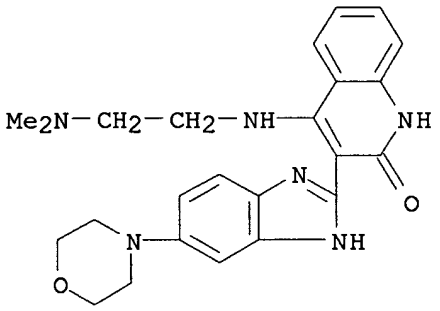


RN 405168-29-8 CAPLUS

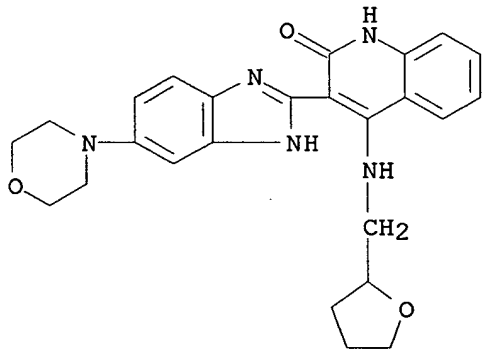
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



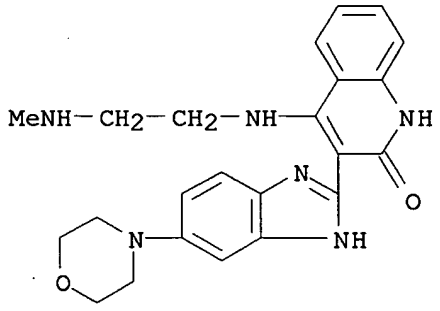
RN 405168-30-1 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(dimethylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



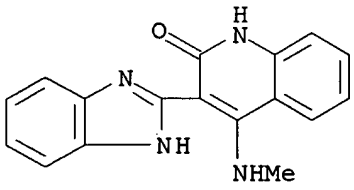
RN 405168-31-2 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



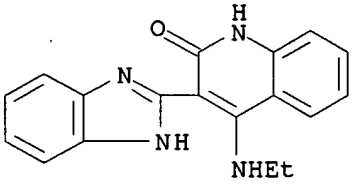
RN 405168-32-3 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(methylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



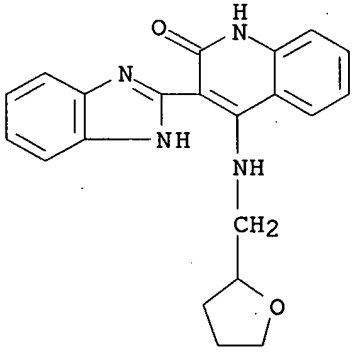
RN 405168-38-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(methylamino)- (9CI) (CA INDEX NAME)



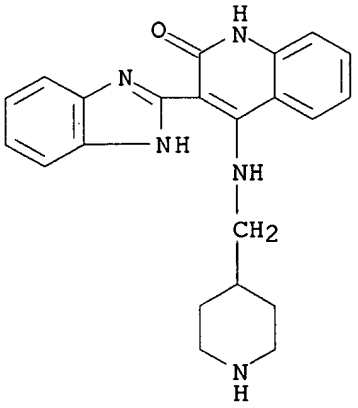
RN 405168-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(ethylamino)- (9CI) (CA INDEX NAME)



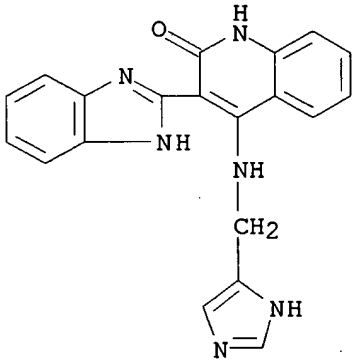
RN 405168-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



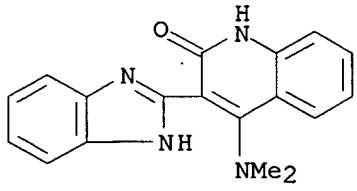
RN 405168-41-4 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



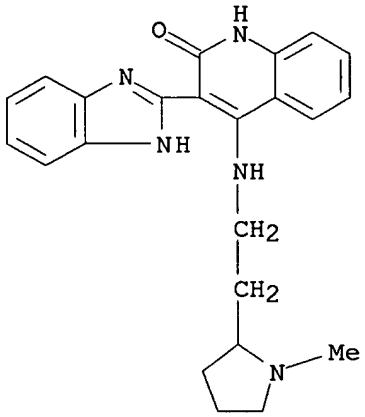
RN 405168-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-4-ylmethyl)amino]- (9CI) (CA INDEX NAME)



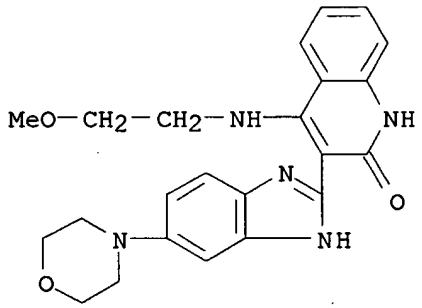
RN 405170-04-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA INDEX NAME)



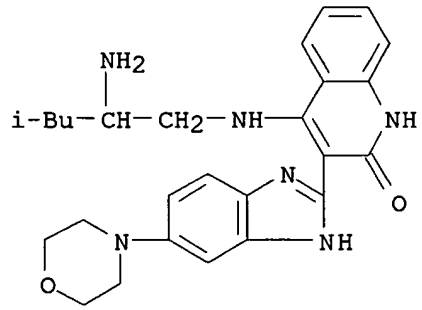
RN 405170-84-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



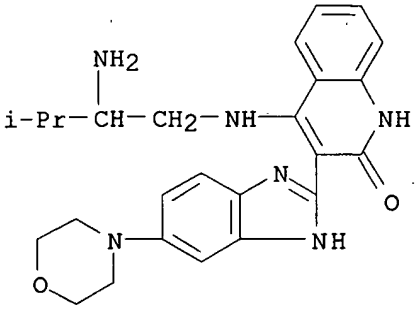
RN 405170-85-6 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



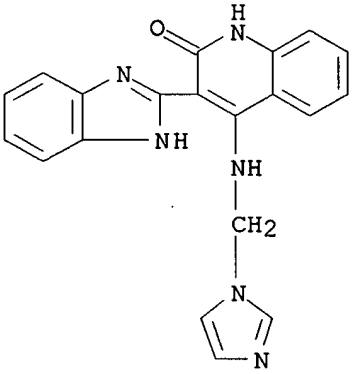
RN 405170-86-7 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-4-methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



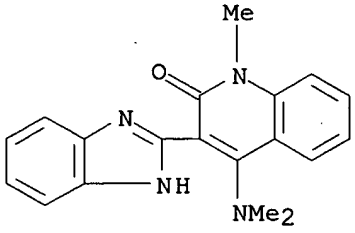
RN 405170-87-8 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



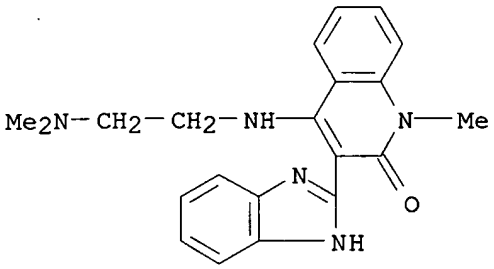
RN 668422-85-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-1-ylmethyl)amino]- (9CI) (CA INDEX NAME)



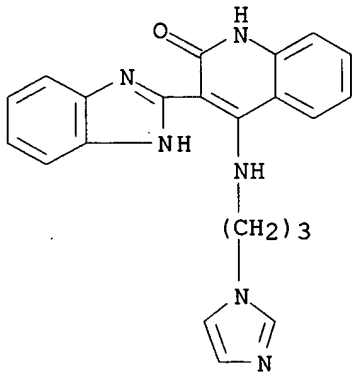
RN 668423-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)-1-methyl- (9CI) (CA INDEX NAME)



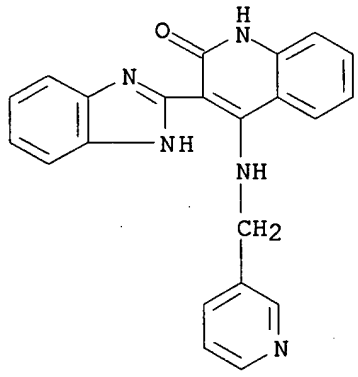
RN 668423-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



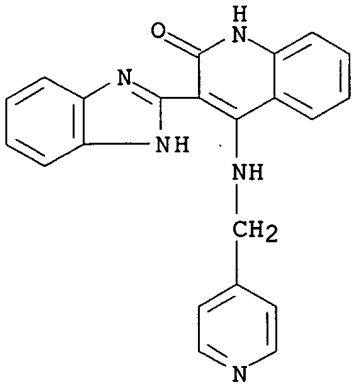
RN 668423-43-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[3-(1H-imidazol-1-yl)propyl]amino]- (9CI) (CA INDEX NAME)



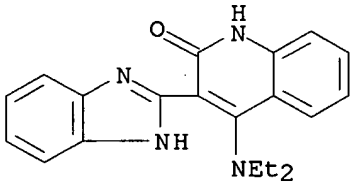
RN 668423-44-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



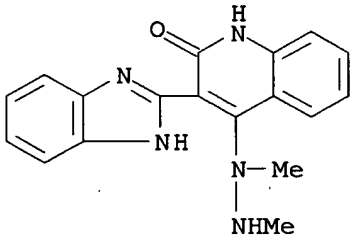
RN 668423-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



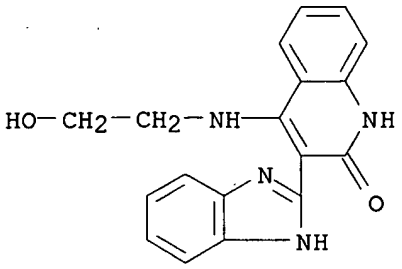
RN 668423-51-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(diethylamino)- (9CI) (CA INDEX NAME)



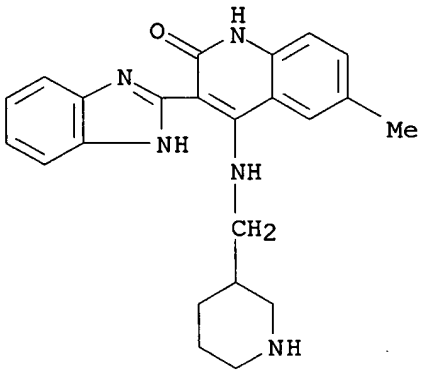
RN 668423-52-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(1,2-dimethylhydrazino)- (9CI) (CA INDEX NAME)



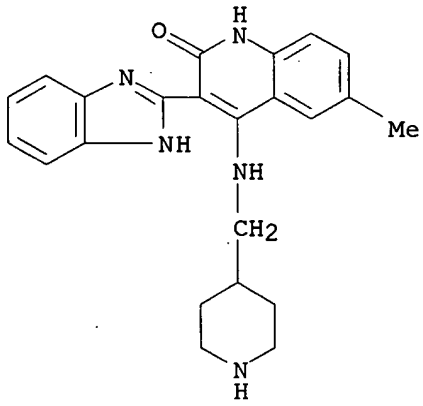
RN 668423-81-2 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(2-hydroxyethyl)amino]- (9CI) (CA INDEX NAME)



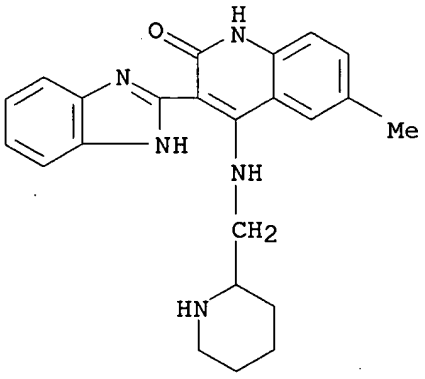
RN 668424-44-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



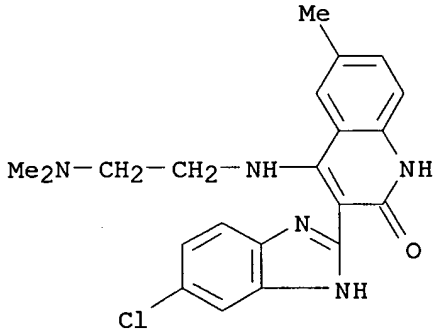
RN 668424-49-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



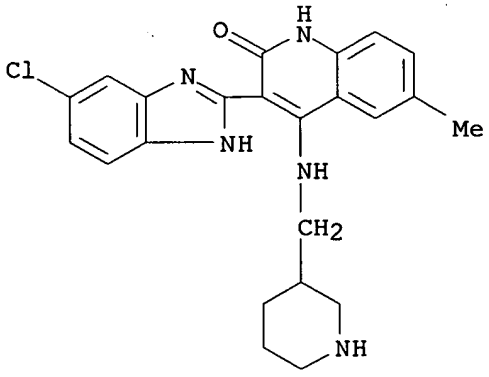
RN 668424-52-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



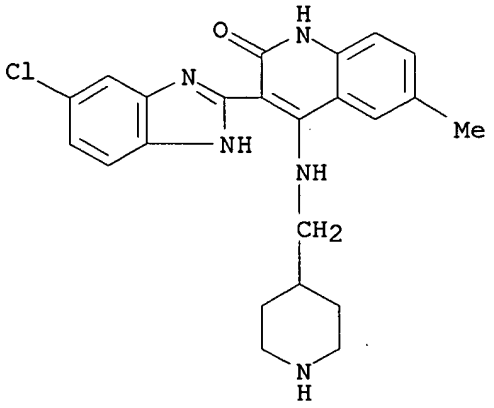
RN 668429-04-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-6-methyl- (9CI) (CA INDEX NAME)



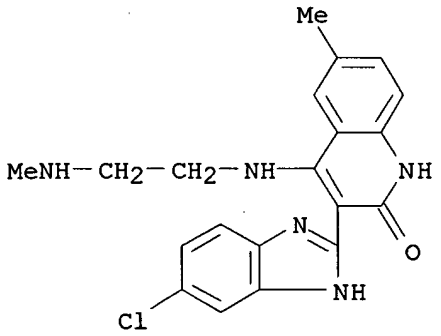
RN 668429-07-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



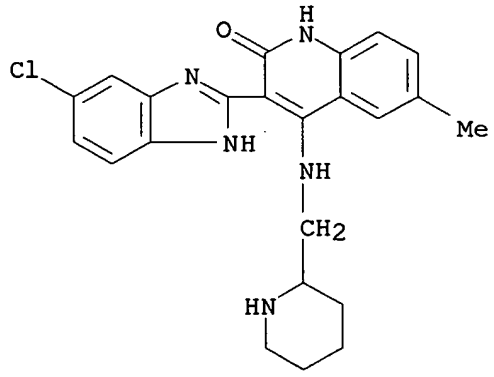
RN 668429-10-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 668429-13-8 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[[2-(methylamino)ethyl]amino]- (9CI) (CA INDEX NAME)



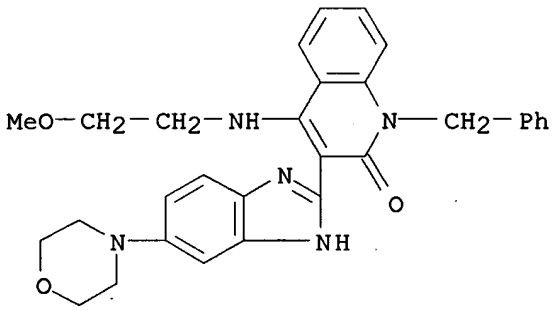
RN 668429-15-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



IT 405171-07-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of benzimidazole quinolinones for inhibiting a checkpoint kinase 1 and their use in combination therapy for cancer)

RN 405171-07-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:976928 CAPLUS
DN 143:279443
TI 4-Amino-3-(benzimidazol-2-yl)quinolin-2-one derivatives for the modulation of inflammatory and metastatic processes
IN Lee, Sang H.; Heise, Carla C.
PA Chiron Corporation, USA
SO PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005082340	A2	20050909	WO 2005-US5316	20050218
	WO 2005082340	A3	20060504		
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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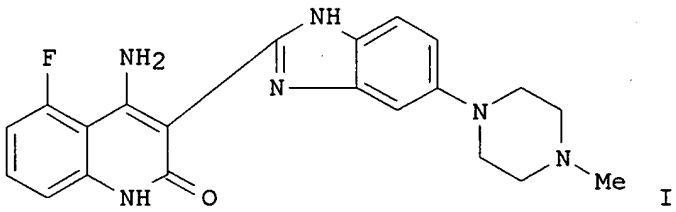
	CA 2556872	AA	20050909	CA 2005-2556872	20050218
	US 2005239825	A1	20051027	US 2005-61386	20050218
PRAI	US 2004-546395P	P	20040220		
	US 2004-547103P	P	20040223		
	US 2004-554771P	P	20040319		
	WO 2005-US5316	W	20050218		

Later

OS MARPAT 143:279443
GI



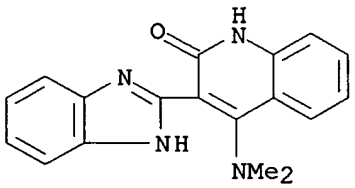
I

AB The invention provides methods for using of using 4-Amino-3-(benzimidazol-2-yl)quinolin-2-one derivs. (Markush included), or a salt or tautomer thereof, in the treatment of disorders relating to cell adhesion and metastatic processes. Preparation of I is included.

IT 405170-04-9 405170-84-5 668423-39-0
668423-40-3 668423-43-6 668423-44-7
668423-47-0 668423-51-6 668423-52-7
668423-81-2 668424-44-0 668424-49-5
668424-52-0 668429-04-7 668429-07-0
668429-10-5 668429-13-8 668429-15-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzimidazolyl aminoquinolinone derivs. for modulation of inflammatory and metastatic processes)

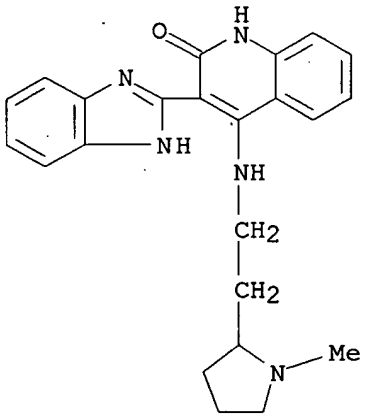
RN 405170-04-9 CAPLUS

CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA INDEX NAME)

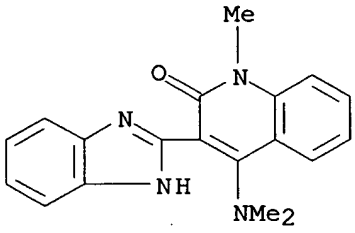


RN 405170-84-5 CAPLUS

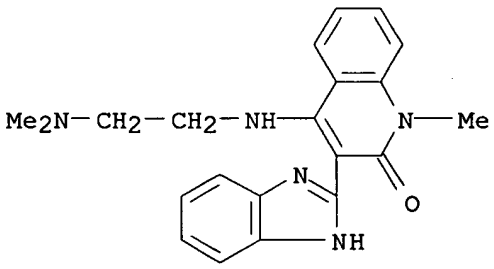
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



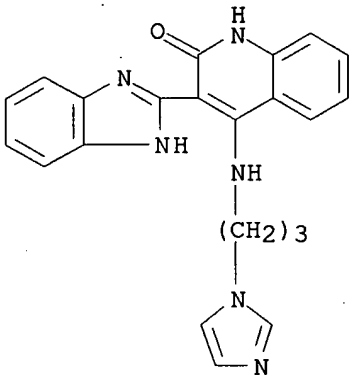
RN 668423-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)-1-methyl- (9CI) (CA INDEX NAME)



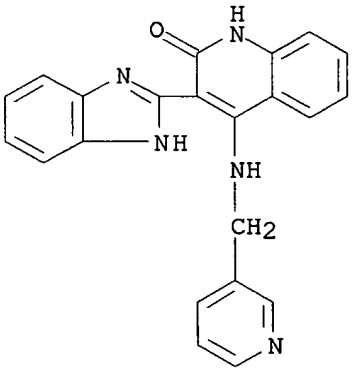
RN 668423-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



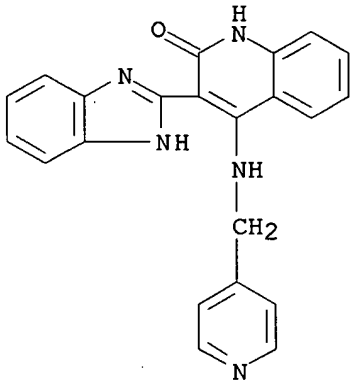
RN 668423-43-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[3-(1H-imidazol-1-yl)propyl]amino]- (9CI) (CA INDEX NAME)



RN 668423-44-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(3-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)

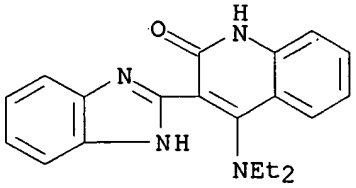


RN 668423-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)

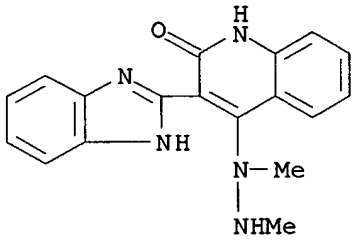


RN 668423-51-6 CAPLUS

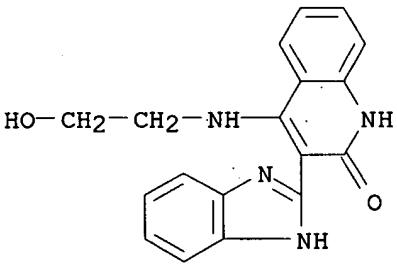
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(diethylamino)- (9CI) (CA INDEX NAME)



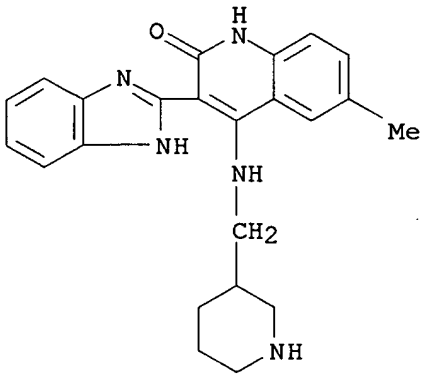
RN 668423-52-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(1,2-dimethylhydrazino)- (9CI) (CA INDEX NAME)



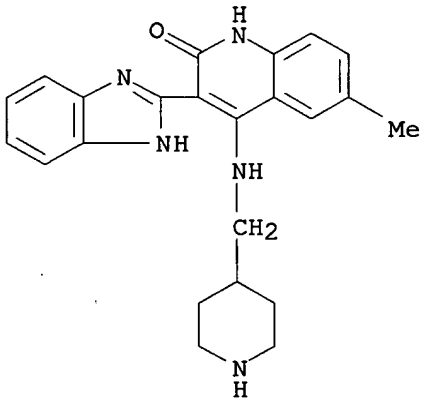
RN 668423-81-2 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(2-hydroxyethyl)amino]- (9CI) (CA INDEX NAME)



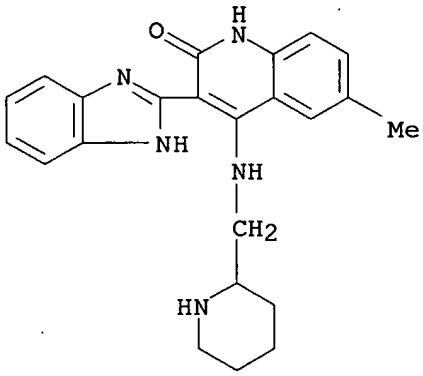
RN 668424-44-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 668424-49-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

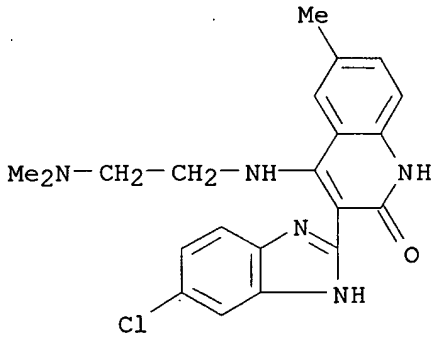


RN 668424-52-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

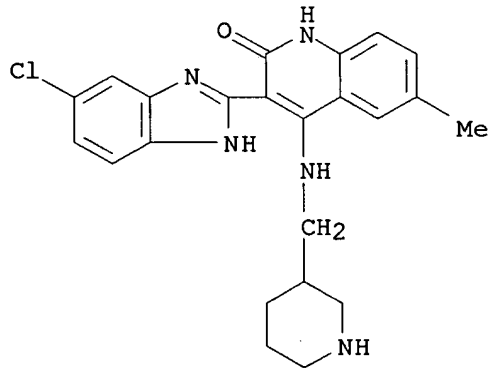


RN 668429-04-7 CAPLUS

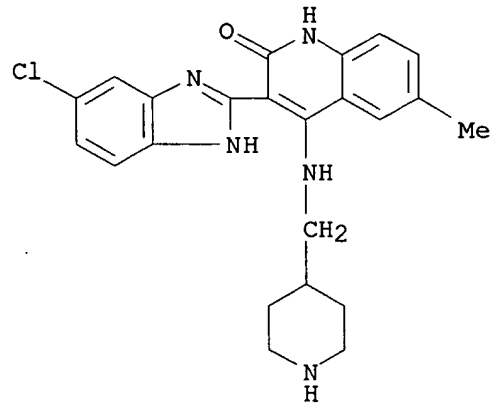
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-6-methyl- (9CI) (CA INDEX NAME)



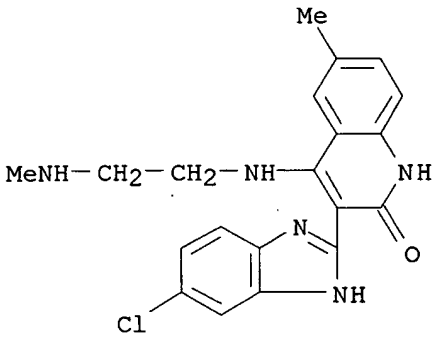
RN 668429-07-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



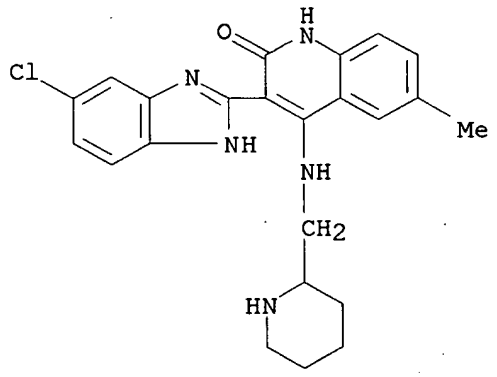
RN 668429-10-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 668429-13-8 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[[2-(methylamino)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 668429-15-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



L9 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:451351 CAPLUS
DN 143:7710
TI Preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma
IN Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla C.; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Wiesmann, Marion; Zhu, Shuguang
PA Chiron Corporation, USA
SO PCT Int. Appl., 567 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005047244	A2	20050526	WO 2004-US36956	20041105

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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CA 2544186	AA	20050526	CA 2004-2544186	20041105
US 2005137399	A1	20050623	US 2004-982757	20041105
US 2005209247	A1	20050922	US 2004-982543	20041105
EP 1692085	A2	20060823	EP 2004-810419	20041105

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PRAI US 2003-517915P	P	20031107	
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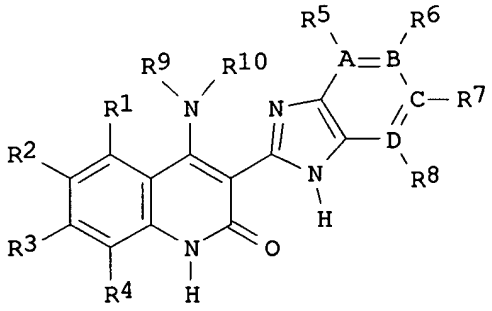
US 2004-546017P	P	20040219	
WO 2004-US36956	W	20041105	

Later

OS MARPAT 143:7710

GI



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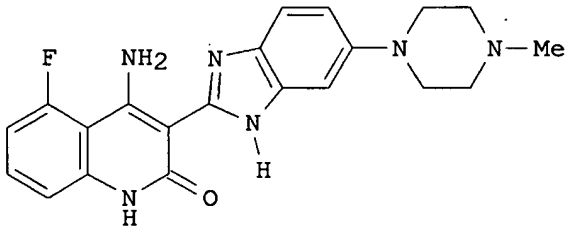


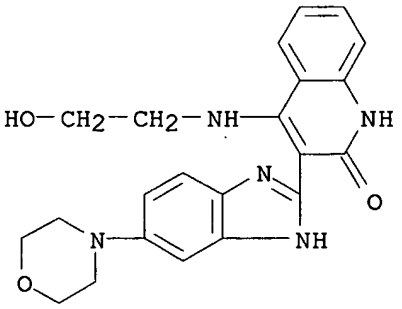
II

AB The title compds. I [A, B, C, and D = C, N; R1-R3 = H, halo, CN, NO2, etc.; R4 = H, alkyl; R5-R8 = H, halo, CN, NO2, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H], useful for inhibiting fibroblast growth factor receptor 3 or treating a biol. condition mediated

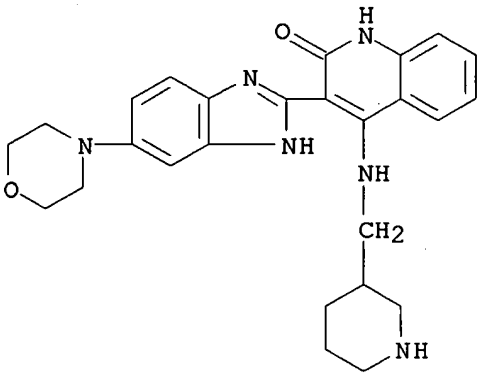
by fibroblast growth factor receptor 3, were prepared E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one (II), starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM. The mentioned above compound II was tested in various tests and showed significant antiproliferative activity. II inhibits FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

IT 405168-26-5P 405168-29-8P 405168-30-1P
405168-31-2P 405168-32-3P 405168-38-9P
405168-39-0P 405168-40-3P 405168-41-4P
405168-47-0P 405170-04-9P 405170-84-5P
405170-85-6P 405170-86-7P 405170-87-8P
668422-85-3P 668423-39-0P 668423-40-3P
668423-43-6P 668423-44-7P 668423-47-0P
668423-51-6P 668423-52-7P 668423-81-2P
668424-44-0P 668424-49-5P 668424-52-0P
668429-04-7P 668429-07-0P 668429-10-5P
668429-13-8P 668429-15-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma)

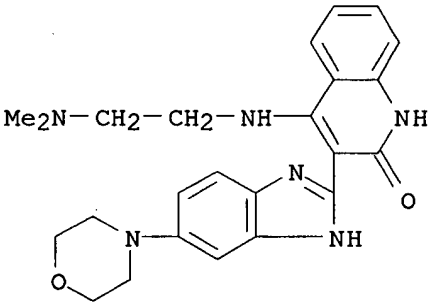
RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



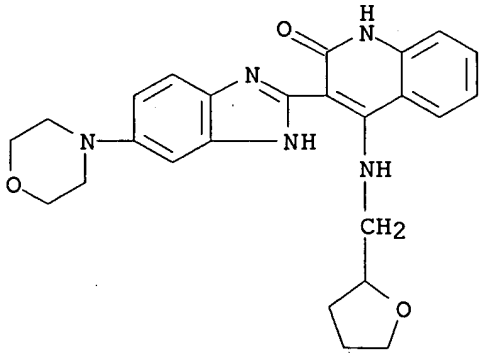
RN 405168-29-8 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



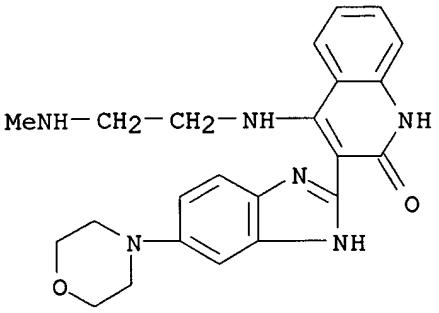
RN 405168-30-1 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(dimethylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



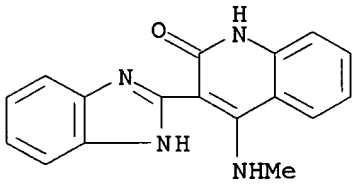
RN 405168-31-2 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



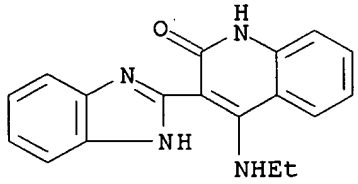
RN 405168-32-3 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(methylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



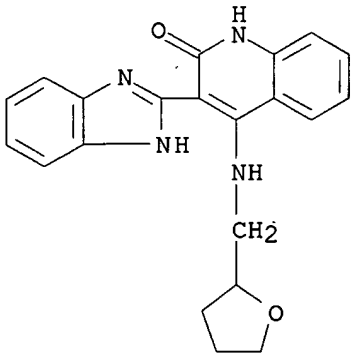
RN 405168-38-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(methylamino)- (9CI) (CA INDEX NAME)



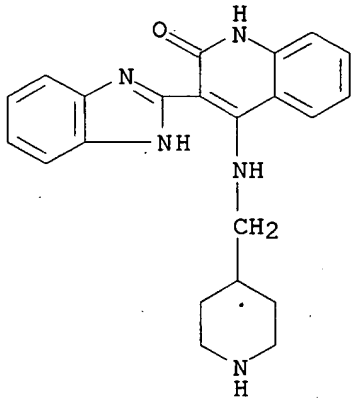
RN 405168-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(ethylamino)- (9CI) (CA INDEX NAME)



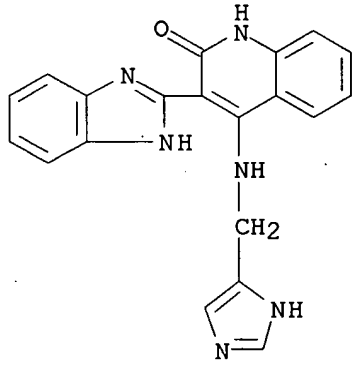
RN 405168-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 405168-41-4 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

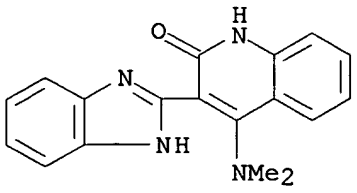


RN 405168-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-4-ylmethyl)amino]- (9CI) (CA INDEX NAME)

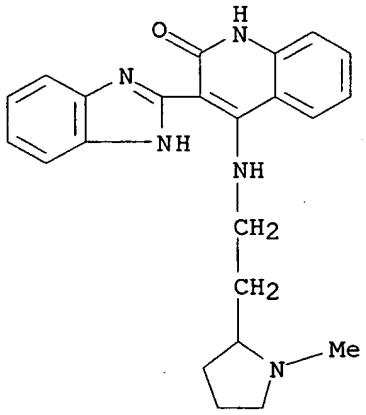


RN 405170-04-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA

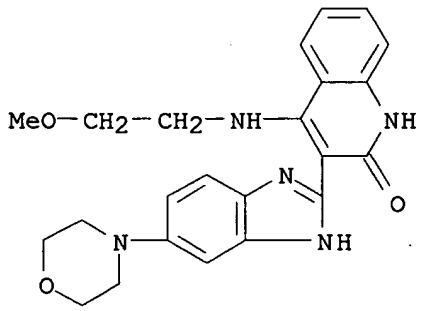
INDEX NAME)



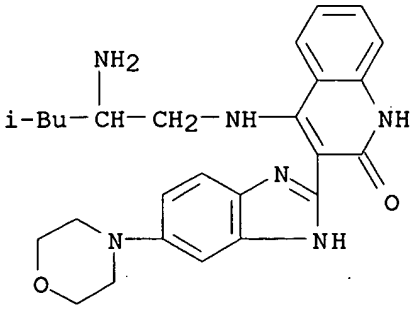
RN 405170-84-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



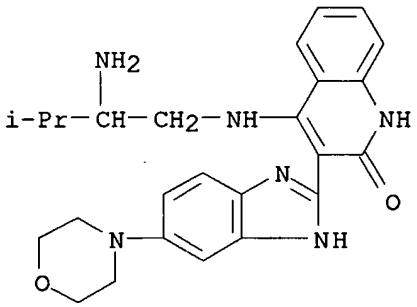
RN 405170-85-6 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



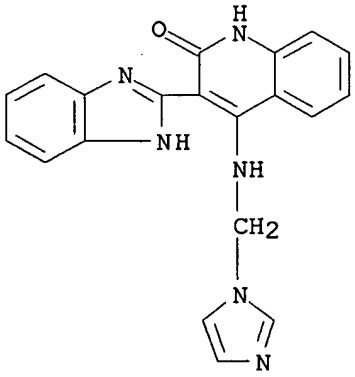
RN 405170-86-7 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-4-methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



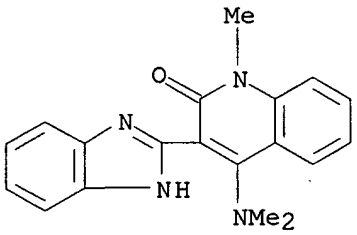
RN 405170-87-8 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



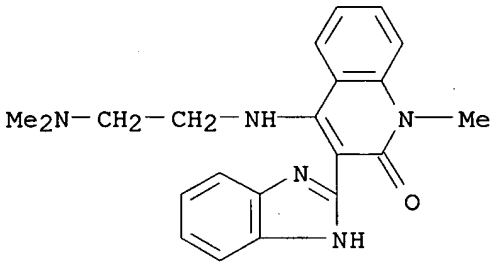
RN 668422-85-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-1-ylmethyl)amino]- (9CI) (CA INDEX NAME)



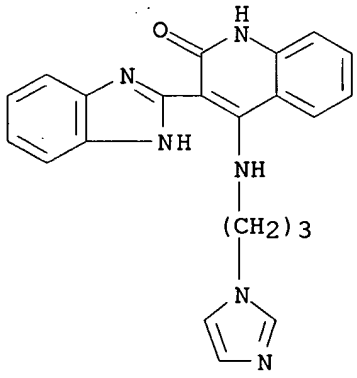
RN 668423-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)-1-methyl-(9CI) (CA INDEX NAME)



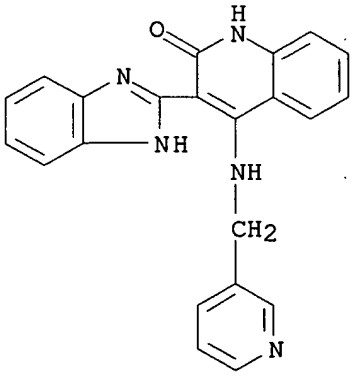
RN 668423-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



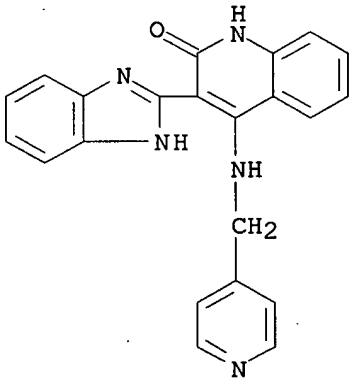
RN 668423-43-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[3-(1H-imidazol-1-yl)propyl]amino]- (9CI) (CA INDEX NAME)



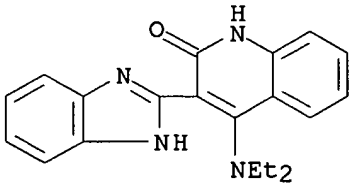
RN 668423-44-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(3-pyridinylmethyl)amino]-(9CI) (CA INDEX NAME)



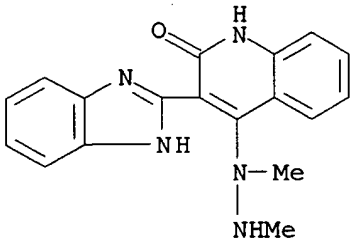
RN 668423-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



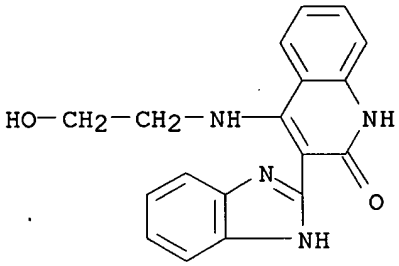
RN 668423-51-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(diethylamino)- (9CI) (CA INDEX NAME)



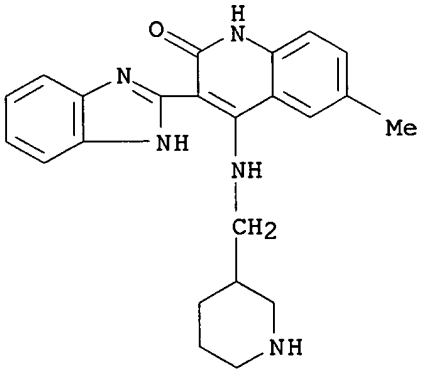
RN 668423-52-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(1,2-dimethylhydrazino)- (9CI) (CA INDEX NAME)



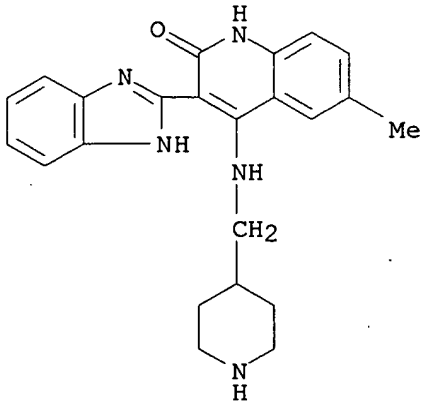
RN 668423-81-2 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(2-hydroxyethyl)amino]- (9CI) (CA INDEX NAME)



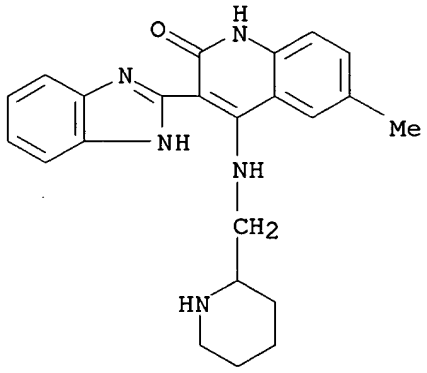
RN 668424-44-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



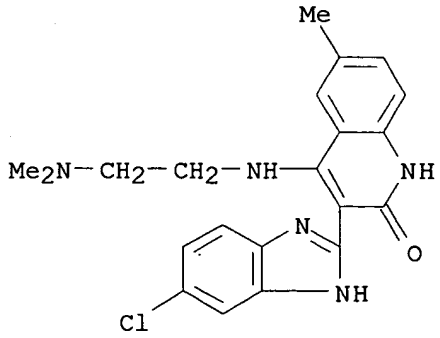
RN 668424-49-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 668424-52-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

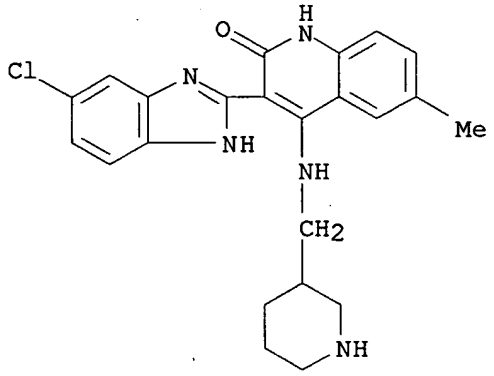


RN 668429-04-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-6-methyl- (9CI) (CA INDEX NAME)

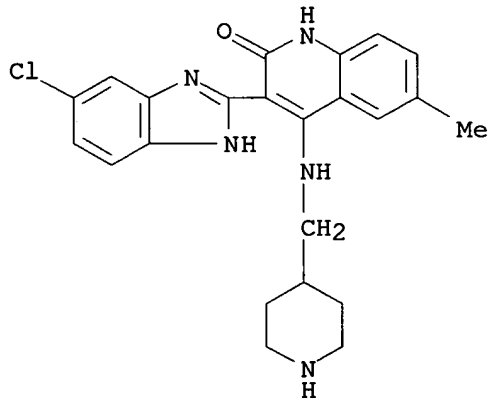


RN 668429-07-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(3-

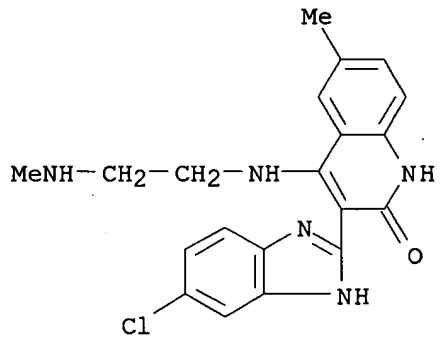
piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



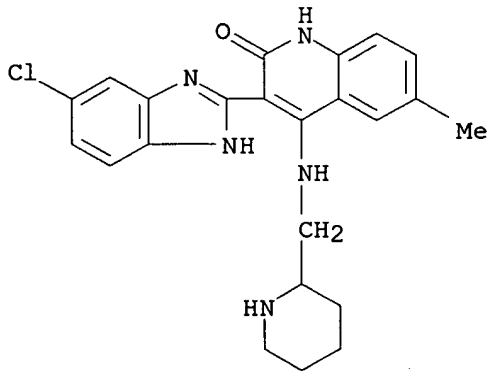
RN 668429-10-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



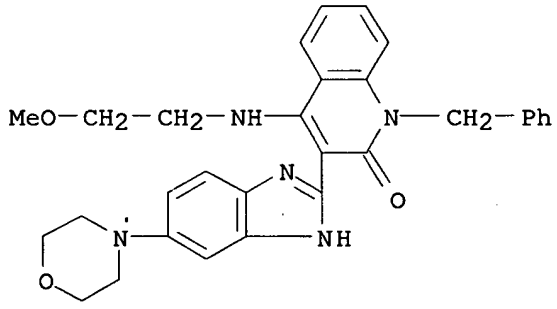
RN 668429-13-8 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[[2-(methylamino)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 668429-15-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



IT 405171-07-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma)
RN 405171-07-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:451118 CAPLUS
DN 143:7709
TI Preparation of benzimidazole quinolinones and lactate salts thereof for inhibiting vascular endothelial growth factor receptor tyrosine kinase
IN Cai, Shaopei; Chou, Joyce; Harwood, Eric; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Zhu, Shuguang
PA Chiron Corporation, USA
SO PCT Int. Appl., 215 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2005046589	A2	20050526	WO 2004-US36941	20041105
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	US 2003-526425P	P	20031202		
	US 2003-526426P	P	20031202		
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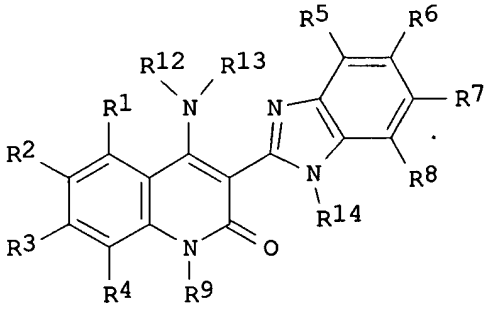
OS CASREACT 143:7709; MARPAT 143:7709

GI



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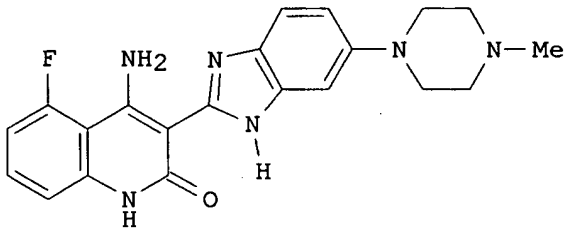

II

AB The title compds. I [R1-R4 = H, halo, CN, NO2, etc.; R5-R8 = H, halo, NO2,

etc.; R9 = H; R12 = H, alkyl, aryl, heterocyclyl; R13 = H, alkyl, aryl, heterocyclyl, etc.; R14 = H] and their pharmaceutically acceptable lactate salts, useful for inhibiting vascular endothelial growth factor receptor tyrosine kinase, were prepared E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one (II) and its lactate salt, starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The pharmaceutically acceptable salts of I have improved aqueous solubility and desirable drug substance properties. Many of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to Flt-1, KDR, PDGF, c-KIT, FLT-3, VEGFR1, VEGFR2, c-Met, CSF-1, FGFR3 and/or bFGFR. In addition, many of the exemplary compds. exhibited IC50 value of less than 10 μM with respect to PDGFR. The 4-amino substituted compds. I such as II were found to be potent inhibitors of various kinases such as VEGFR2 (KDR, Flk-1), FGFR1 and PDGFRβ with IC50's ranging from 10-27 nM. II inhibits FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

IT 405170-04-9P 405170-84-5P 668423-39-0P
668423-40-3P 668423-43-6P 668423-44-7P
668423-47-0P 668423-51-6P 668423-52-7P
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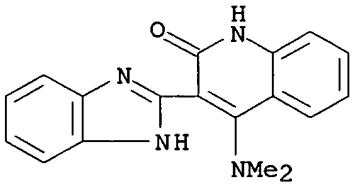
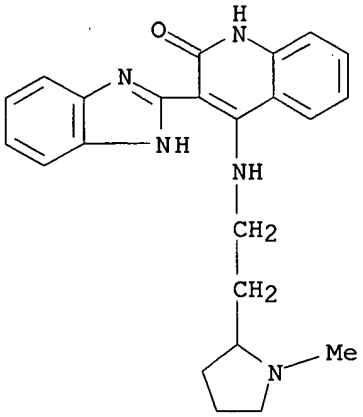
668424-52-0P 668429-04-7P 668429-07-0P
668429-10-5P 668429-13-8P 668429-15-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones and lactate salts thereof for inhibiting vascular endothelial growth factor receptor tyrosine kinase)

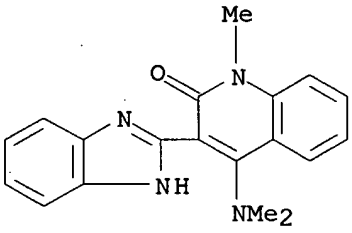
RN 405170-04-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA INDEX NAME)



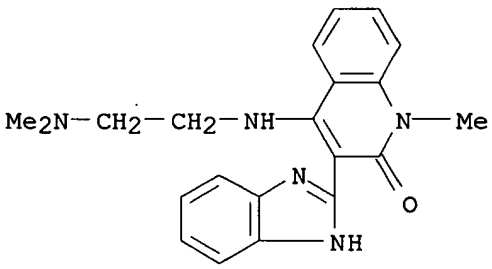
RN 405170-84-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



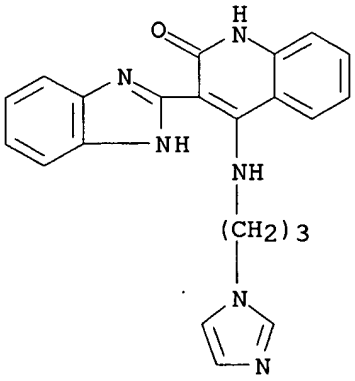
RN 668423-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)-1-methyl- (9CI) (CA INDEX NAME)



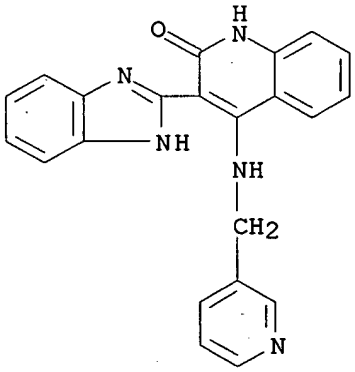
RN 668423-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



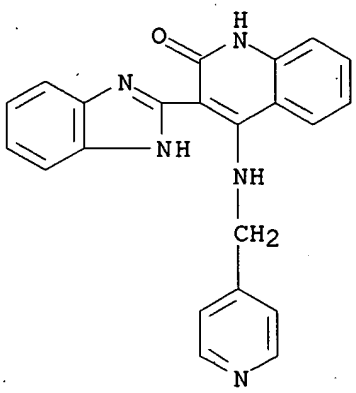
RN 668423-43-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[3-(1H-imidazol-1-yl)propyl]amino]- (9CI) (CA INDEX NAME)



RN 668423-44-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(3-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)

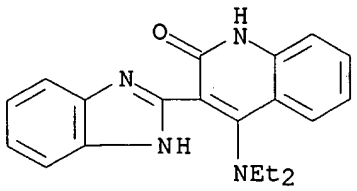


RN 668423-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)

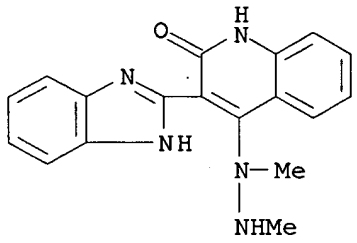


RN 668423-51-6 CAPLUS

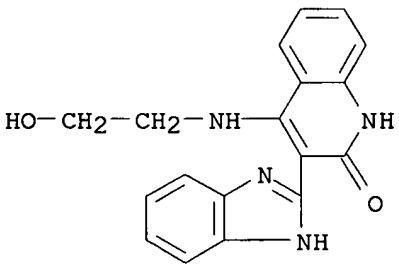
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(diethylamino)- (9CI) (CA INDEX NAME)



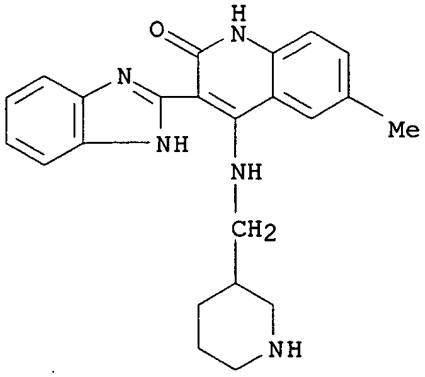
RN 668423-52-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(1,2-dimethylhydrazino)- (9CI) (CA INDEX NAME)



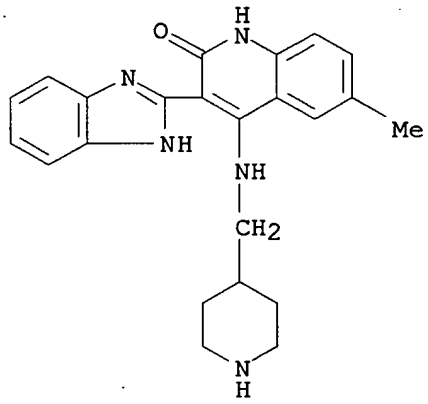
RN 668423-81-2 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(2-hydroxyethyl)amino]- (9CI) (CA INDEX NAME)



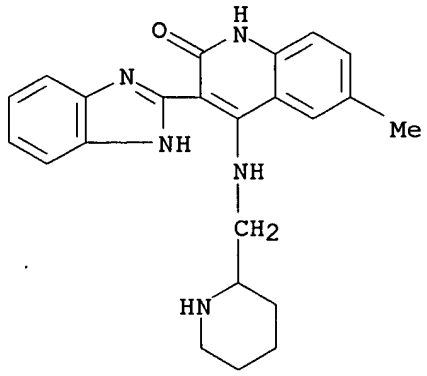
RN 668424-44-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 668424-49-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

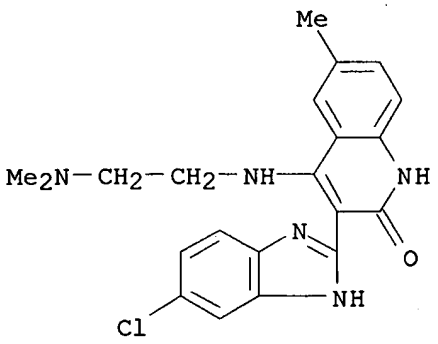


RN 668424-52-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

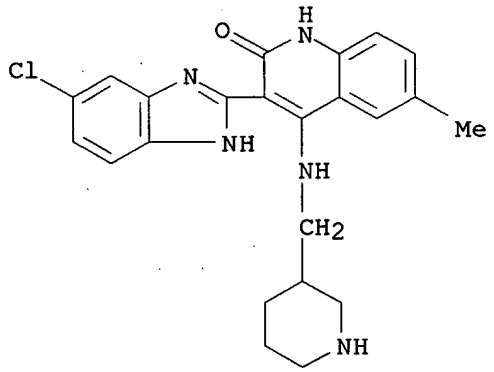


RN 668429-04-7 CAPLUS

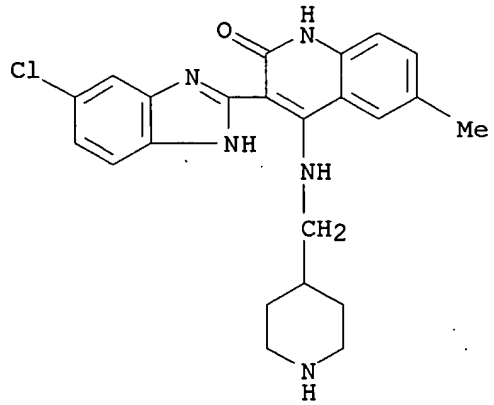
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-6-methyl- (9CI) (CA INDEX NAME)



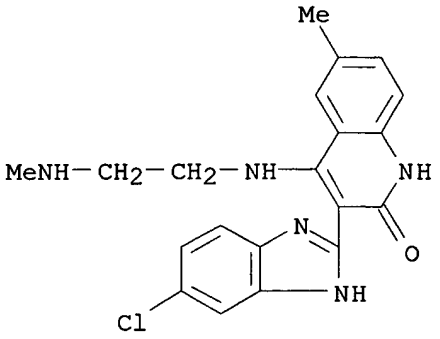
RN 668429-07-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



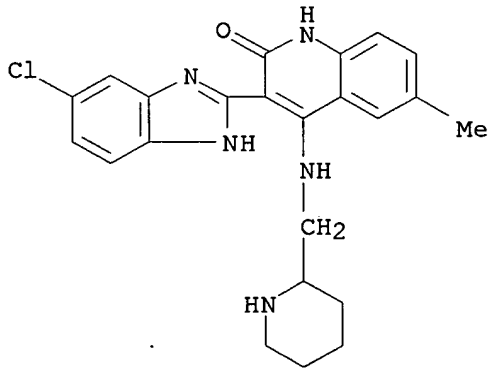
RN 668429-10-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 668429-13-8 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[[2-(methylamino)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 668429-15-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



L9 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:310953 CAPLUS
DN 140:321363
TI Preparation of [(piperazinyl)benzimidazolyl]quinolinones and analogs as tyrosine kinase inhibitors for treatment of cancer
IN Velaparthi, Upender; Wittman, Mark D.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004030620	A2	20040415	WO 2003-US30669	20030929
	WO 2004030620	A3	20040610		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

Apps

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU	2003275282	A1	20040423	AU 2003-275282	20030929
US	2004092514	A1	20040513	US 2003-674098	20030929
EP	1545529	A2	20050629	EP 2003-759558	20030929

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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRAI	US 2002-415066P	P	20020930
	WO 2003-US30669	W	20030929

OS MARPAT 140:321363
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I and II [wherein A, B, D, and E = independently C, N, O, S or a direct bond, provided that not more than one of A, B, D, and E can be a single bond; Y = O or S; W = N, CH, O, and S, provided that when W = O or S, R7 is absent; R1-R7 = independently H, alkyl, alkenyl, alkynyl, (hetero)cycloalkyl, halo, amino(alkyl), (thio)alkoxy, NO2, (hetero)aryl, (thio)alkoxyalkyl, aminoalkyl, (hetero)aralkyl, heterocycloalkylalkyl, CN, CO2R8, CONR9R10, CO2NR11R12, NR13CONR14R15, NR16SO2R17, SO2NR18R19, C(NR20)NR21R22, NHZ, or NHZ-(hetero)aryl; Z = (un)substituted (cyclo)alkyl, (cyclo)alkenyl, or alkynyl, optionally interrupted by CO, CONH, CNOR26, CNNR27, CNNCOR28, or CNNSO2R29; R8-R24 and R26 = independently H, alkyl, alkenyl, alkynyl, cycloalkyl(alkyl), OH, alkoxy, (hetero)aryl, heterocyclyl, heteroarylalkyl, alkyl-R25; R25 = alkenyl, OH, SH, (thio)alkoxy, NH2, (di)alkylamino, (hetero)aryl, CN, halo, heterocyclyl, sulfoxy, sulfonyl, NR27CO2R28, NR29COR30, NR31SO2R32, SO2NR31R32, or CONR33R34; R27-R34 = independently H, or (cyclo)alkyl; and enantiomers, diastereomers, pharmaceutically acceptable salts, hydrates, prodrugs, or solvates thereof] were prepared as tyrosine kinase inhibitors. For example, 1-[4-(3,4-diamino-5-methylphenyl)piperazin-1-yl]ethanone was condensed with 2,4-dichloroquinoline-3-carboxaldehyde in MeOH to give the benzimidazole. Hydrolysis of the chloro group using 4N HCl in dioxane afforded the 2- and 4-quinolinones. Nucleophilic addition of (S)-2-(3-chlorophenyl)-2-hydroxyethylamine using N-methylmorpholine in DMF provided III and IV. Compds. of the invention exhibited kinase activity of <25 μM against one or more of the following kinases: CDK, EMT, FAK, Her1, Her2, IGF, IR, LCK, MET, PDGF, VEGF. Thus, I, II, and their pharmaceutical compns. are useful as for treatment of cancer and other diseases that can be treated by inhibiting tyrosine kinase enzymes (no data).

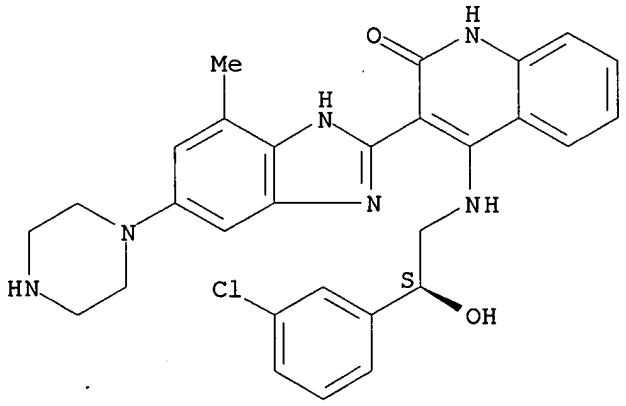
IT 677341-90-1P, 4-[[(S)-2-(3-Chlorophenyl)-2-hydroxyethyl]amino]-3-[4-methyl-6-(piperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(tyrosine kinase inhibitor; preparation of [(piperazinyl)benzimidazolyl]quin

olinones and analogs as tyrosine kinase inhibitors for treatment of cancer)

RN 677341-90-1 CAPLUS

CN 2(1H)-Quinolinone, 4-[[(2S)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-3-[4-methyl-6-(1-piperazinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 677341-88-7P, 3-[6-(4-Acetylpiperazin-1-yl)-4-methyl-1H-benzimidazol-2-yl]-4-[[(S)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-1H-quinolin-2-one 677341-89-8P, 3-[6-(4-Acetylpiperazin-1-yl)-4-methyl-1H-benzimidazol-2-yl]-2-[[(S)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-1H-quinolin-4-one 677341-91-2P, 2-[[(S)-2-(3-Chlorophenyl)-2-hydroxyethyl]amino]-3-[4-methyl-6-(piperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-4-one 677341-92-3P, 4-[[(S)-2-(3-Chlorophenyl)-2-hydroxyethyl]amino]-3-[6-[4-(2-hydroxyethyl)piperazin-1-yl]-4-methyl-1H-benzimidazol-2-yl]-1H-quinolin-2-one

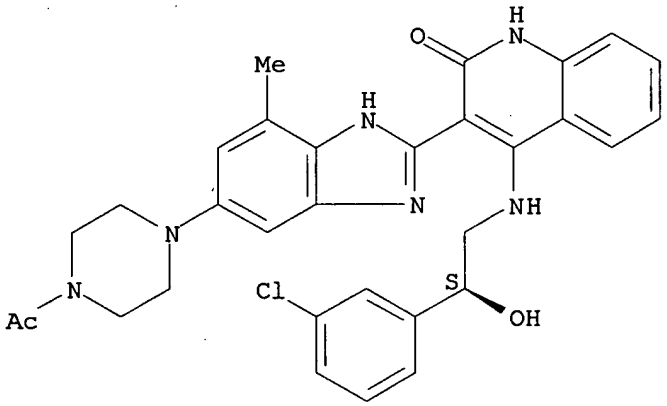
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tyrosine kinase inhibitor; preparation of [(piperazinyl)benzimidazolyl]quinolinones and analogs as tyrosine kinase inhibitors for treatment of cancer)

RN 677341-88-7 CAPLUS

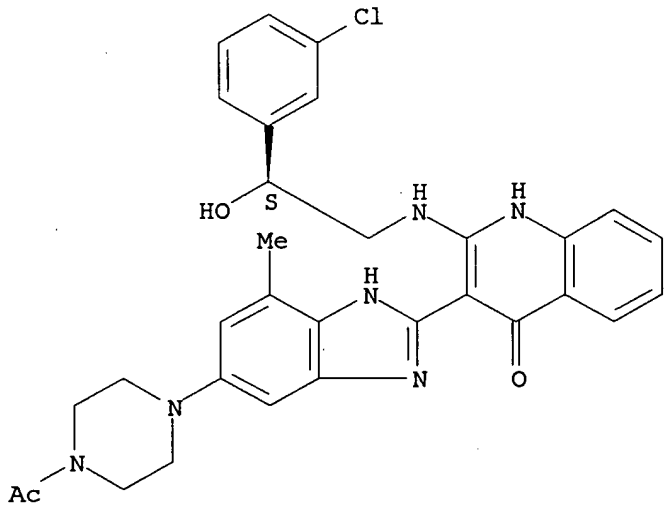
CN Piperazine, 1-acetyl-4-[2-[4-[[(2S)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-1,2-dihydro-2-oxo-3-quinolinyl]-7-methyl-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



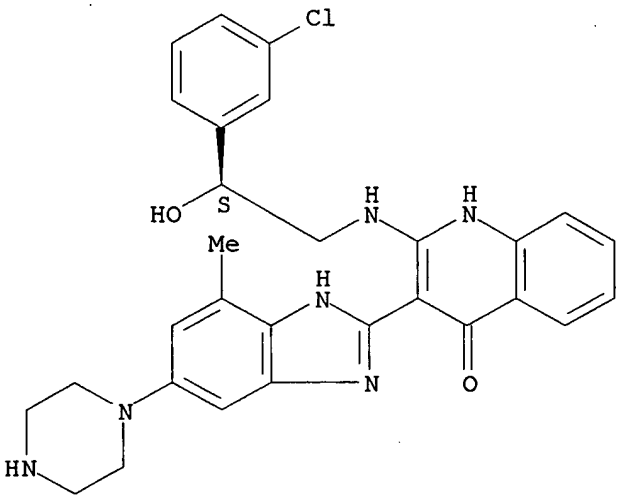
RN 677341-89-8 CAPLUS
CN Piperazine, 1-acetyl-4-[2-[2-[[(2S)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-1,4-dihydro-4-oxo-3-quinolinyl]-7-methyl-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



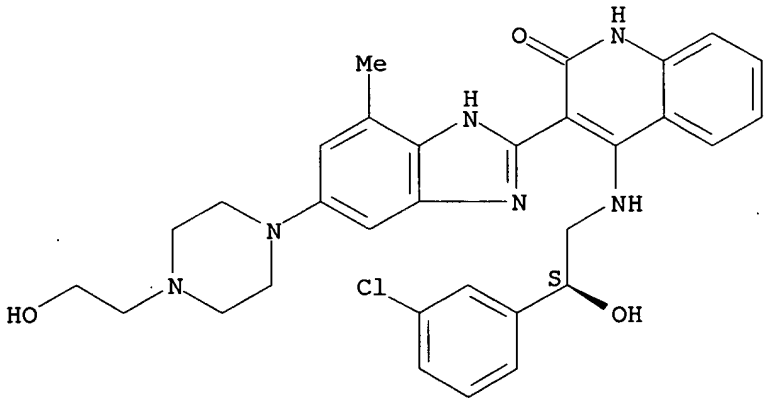
RN 677341-91-2 CAPLUS
CN 4(1H)-Quinolinone, 2-[[(2S)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-3-[4-methyl-6-(1-piperazinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 677341-92-3 CAPLUS
CN 2(1H)-Quinolinone, 4-[[(2S)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-3-[6-[4-(2-hydroxyethyl)-1-piperazinyl]-4-methyl-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:182836 CAPLUS
DN 140:235711
TI Preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase
IN Barsanti, Paul A.; Bussiere, Dirksen; Harrison, Stephen D.; Heise, Carla C.; Jansen, Johanna M.; Jazan, Elisa; Machajewski, Timothy D.; Mcbride, Christopher; McCrea, William R.; Ng, Simon; Ni, Zhi-Jie; Pecchi, Sabina; Pfister, Keith; Ramurthy, Savithri; Renhowe, Paul A.; Shafer, Cynthia M.; Silver, Joel B.; Wagman, Allan; Weismann, Marion
PA Chiron Corporation, USA
SO PCT Int. Appl., 570 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004018419	A2	20040304	WO 2003-US25990	20030819
	WO 2004018419	A3	20040603		
	WO 2004018419	B1	20040729		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	AU 2003288899	A1	20040311	AU 2003-288899	20030819
	EP 1539754	A2	20050615	EP 2003-781286	20030819
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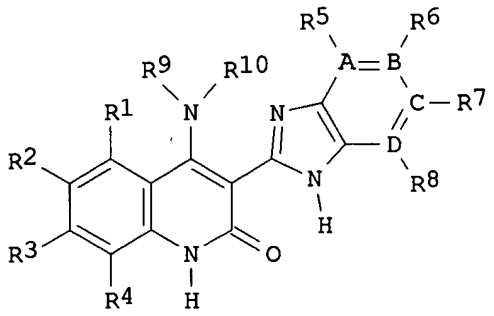
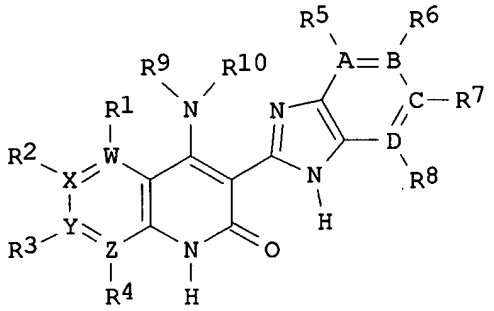
	CN 1692112	A	20051102	CN 2003-824565	20030819
	JP 2006503919	T2	20060202	JP 2005-501762	20030819
PRAI	US 2002-405729P	P	20020823		
	US 2002-426107P	P	20021113		
	US 2002-426226P	P	20021113		
	US 2002-426282P	P	20021113		
	US 2002-428210P	P	20021121		
	US 2003-460327P	P	20030403		
	US 2003-460328P	P	20030403		
	US 2003-460493P	P	20030403		
	US 2003-478916P	P	20030616		
	US 2003-484048P	P	20030701		
	WO 2003-US25990	W	20030819		

OS MARPAT 140:235711
GI



I

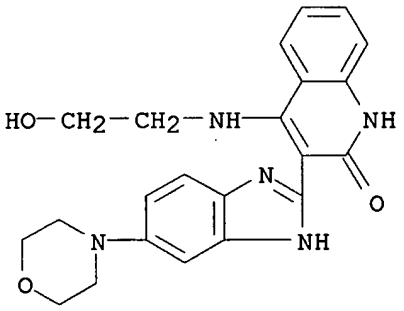


II

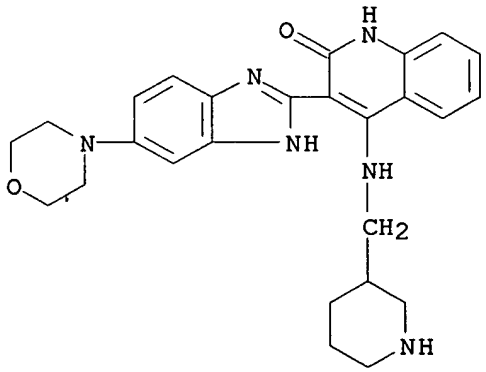
AB The title compds. [I and II; A, B, C, and D = C, N; W, X, Y and Z = C, N and at least one of W, X, Y, and Z = N; R1-R8 = H, halo, CN, NO2, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or NR9R10 = 5-7 membered ring], useful for inhibiting various enzymes and treating various conditions, were prepared E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM.

IT 405168-26-5P 405168-29-8P 405168-30-1P
405168-31-2P 405168-32-3P 405168-38-9P
405168-39-0P 405168-40-3P 405168-41-4P
405168-47-0P 405170-04-9P 405170-84-5P
405170-85-6P 405170-86-7P 405170-87-8P
668422-85-3P 668423-39-0P 668423-40-3P
668423-43-6P 668423-44-7P 668423-47-0P
668423-51-6P 668423-52-7P 668423-81-2P
668424-44-0P 668424-49-5P 668424-52-0P
668429-04-7P 668429-07-0P 668429-10-5P
668429-13-8P 668429-15-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones for inhibiting a serine/threonine

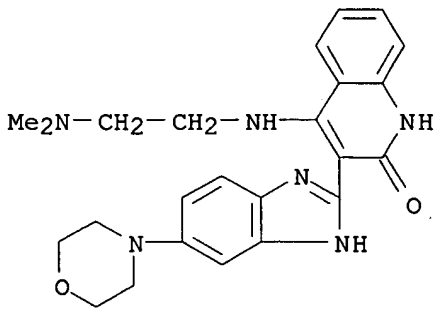
kinase)
RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



RN 405168-29-8 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

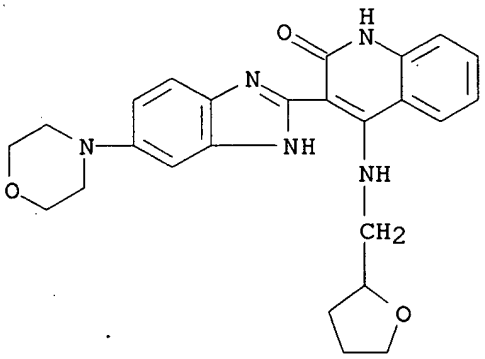


RN 405168-30-1 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(dimethylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

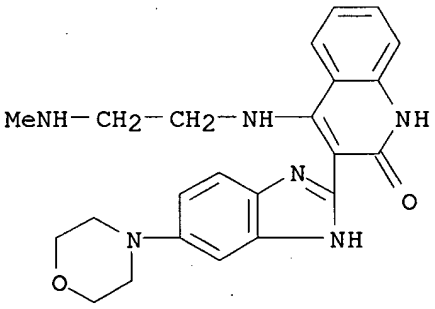


RN 405168-31-2 CAPLUS

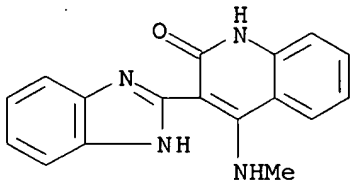
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



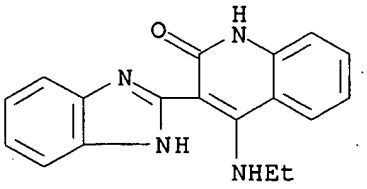
RN 405168-32-3 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(methylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



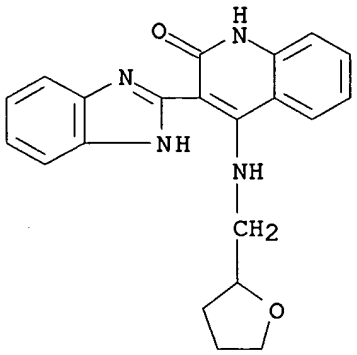
RN 405168-38-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(methylamino)- (9CI) (CA INDEX NAME)



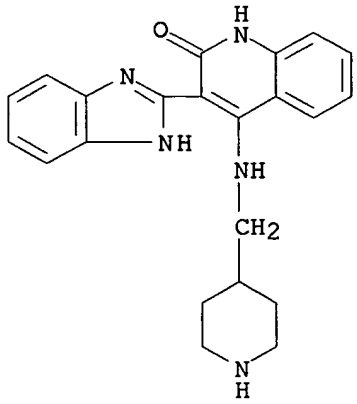
RN 405168-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(ethylamino)- (9CI) (CA INDEX NAME)



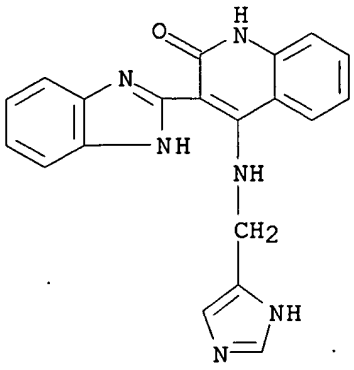
RN 405168-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



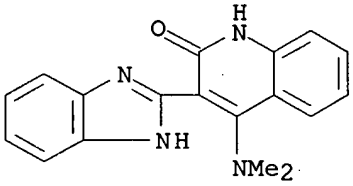
RN 405168-41-4 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



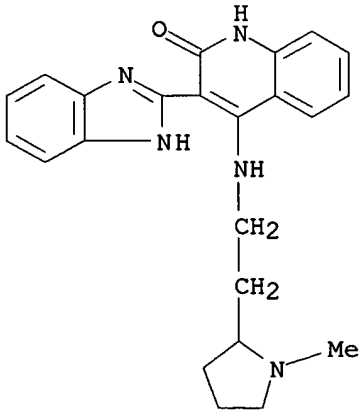
RN 405168-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-4-ylmethyl)amino]- (9CI) (CA INDEX NAME)



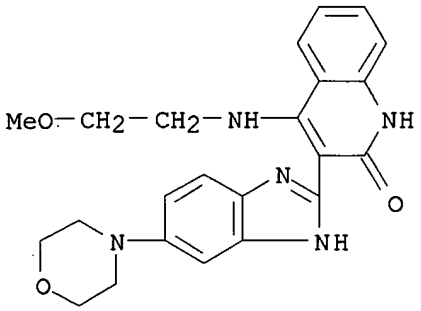
RN 405170-04-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA INDEX NAME)



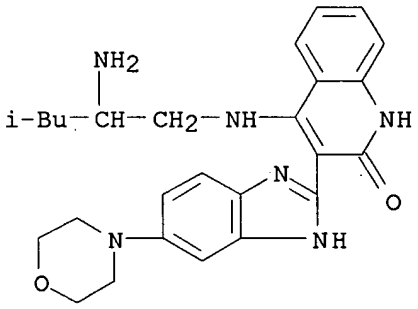
RN 405170-84-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



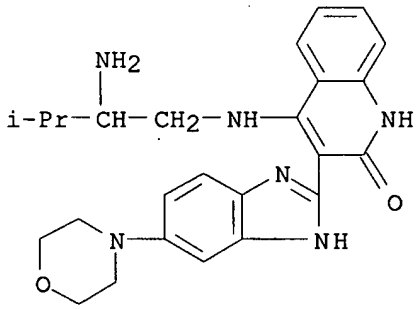
RN 405170-85-6 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



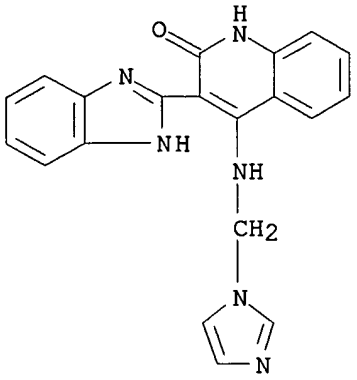
RN 405170-86-7 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-4-methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



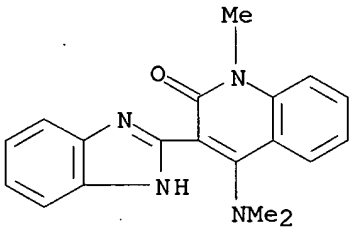
RN 405170-87-8 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



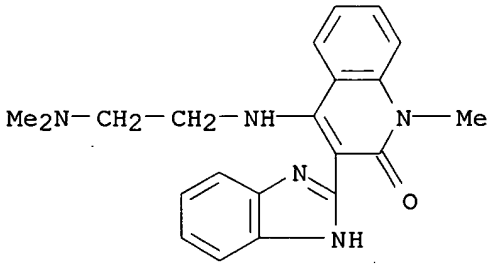
RN 668422-85-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-1-ylmethyl)amino]- (9CI) (CA INDEX NAME)



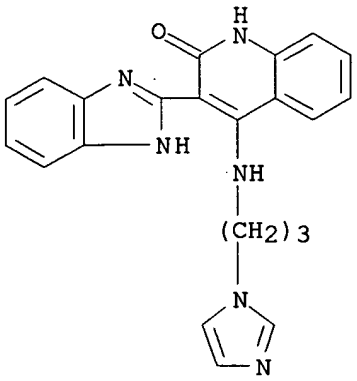
RN 668423-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)-1-methyl- (9CI) (CA INDEX NAME)



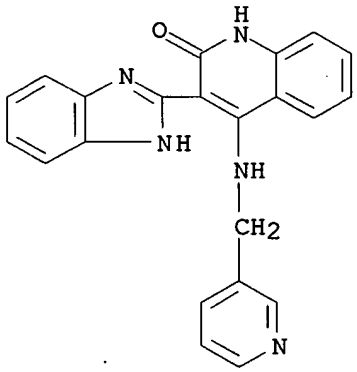
RN 668423-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-1-methyl- (9CI) (CA INDEX NAME)



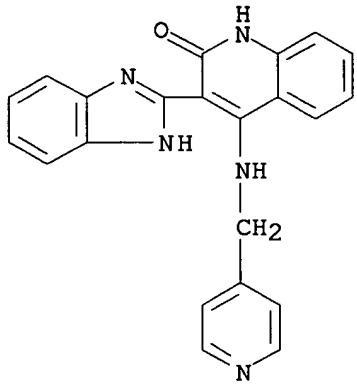
RN 668423-43-6 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[3-(1H-imidazol-1-yl)propyl]amino]- (9CI) (CA INDEX NAME)



RN 668423-44-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(3-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)

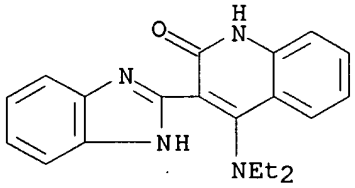


RN 668423-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-pyridinylmethyl)amino]-
(9CI) (CA INDEX NAME)

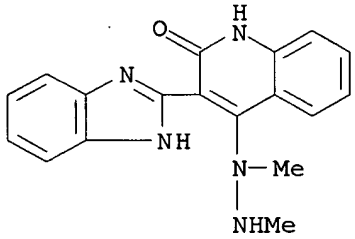


RN 668423-51-6 CAPLUS

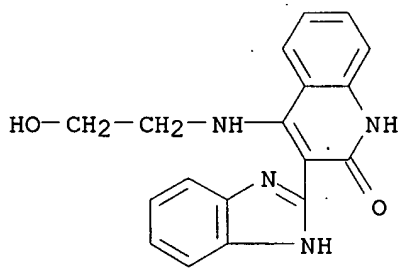
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(diethylamino)- (9CI) (CA INDEX NAME)



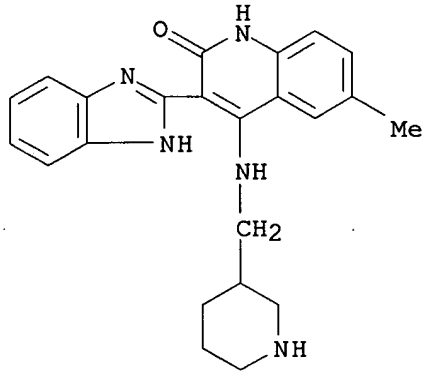
RN 668423-52-7 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(1,2-dimethylhydrazino)- (9CI) (CA INDEX NAME)



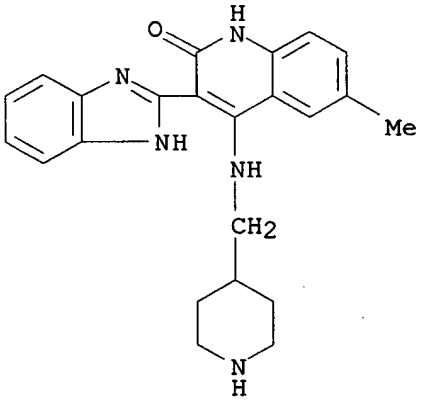
RN 668423-81-2 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(2-hydroxyethyl)amino]- (9CI) (CA INDEX NAME)



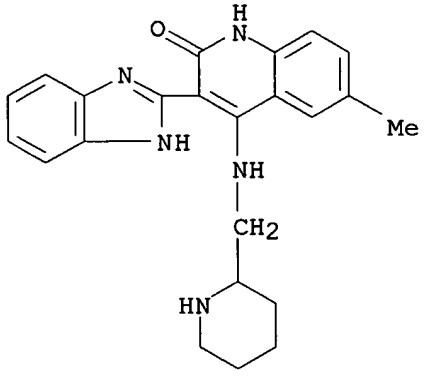
RN 668424-44-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 668424-49-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

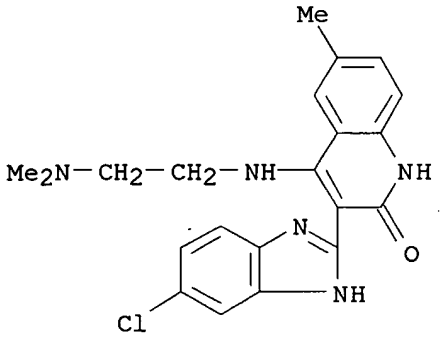


RN 668424-52-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

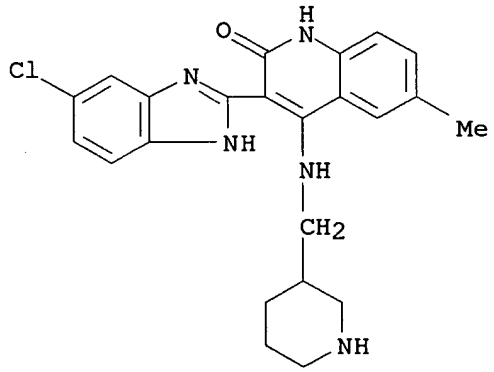


RN 668429-04-7 CAPLUS

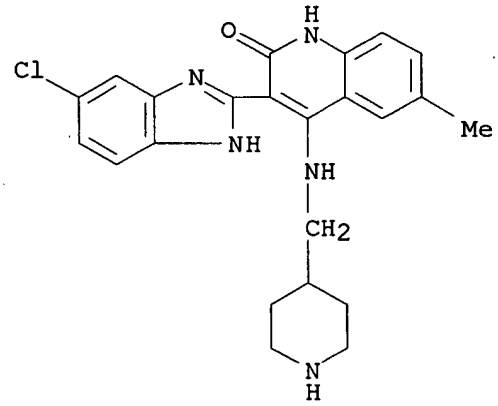
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-4-[[2-(dimethylamino)ethyl]amino]-6-methyl- (9CI) (CA INDEX NAME)



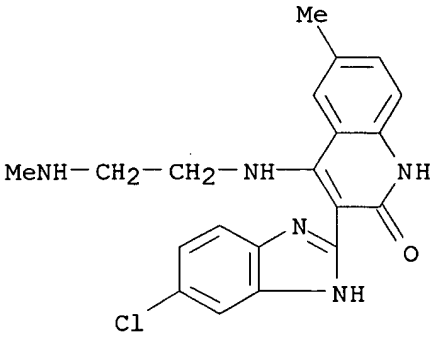
RN 668429-07-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



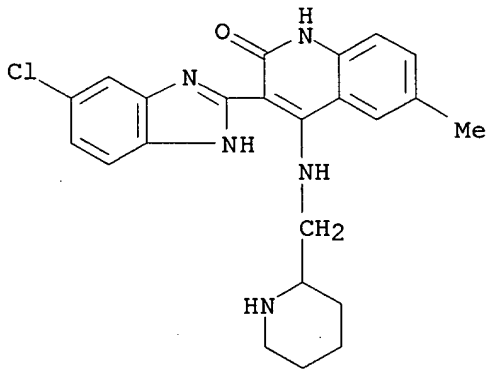
RN 668429-10-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



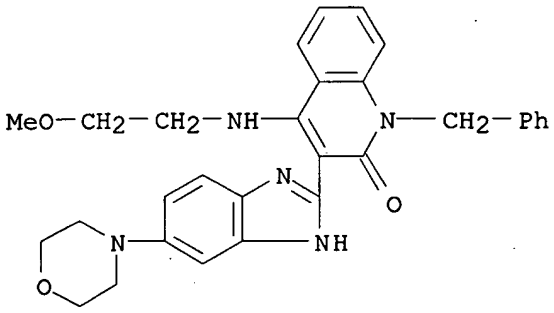
RN 668429-13-8 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[[2-(methylamino)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 668429-15-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(5-chloro-1H-benzimidazol-2-yl)-6-methyl-4-[(2-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



IT 405171-07-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase)
RN 405171-07-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:98039 CAPLUS
DN 138:153534
TI Preparation of benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents
IN Renhowe, Paul A.; Pecchi, Sabina; Machajewski, Timothy D.; Shafer, Cynthia M.; Taylor, Clarke; McCrea, William R.; McBride, Christopher; Jazan, Elisa
PA Chiron Corporation, USA
SO U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U.S. Pat. Appl. 2002 107,392.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003028018	A1	20030206	US 2002-116117	20020405
	US 2002107392	A1	20020808	US 2001-951265	20010911
	US 6605617	B2	20030812		
	EP 1650203	A1	20060426	EP 2005-17665	20010911
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003158224	A1	20030821	US 2002-284017	20021030
	US 6774237	B2	20040810		
	US 2004006101	A1	20040108	US 2003-387355	20030312
	US 6762194	B2	20040713		
	CA 2481055	AA	20031023	CA 2003-2481055	20030404
	WO 2003087095	A1	20031023	WO 2003-US10463	20030404
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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	US 2004097545	A1	20040520	US 2003-613411	20030703
	US 6800760	B2	20041005		
	US 2005054672	A1	20050310	US 2004-886950	20040708
	NO 2004004776	A	20041207	NO 2004-4776	20041103
	US 2005209456	A1	20050922	US 2005-92137	20050329
PRAI	US 2000-232159P	P	20000911		
	US 2001-951265	A2	20010911		
	EP 2001-973722	A3	20010911		
	US 2002-116117	A	20020405		
	US 2002-284017	A1	20021030		
	WO 2003-US10463	W	20030404		
	US 2004-886950	A1	20040708		
OS	MARPAT 138:153534				
GI					

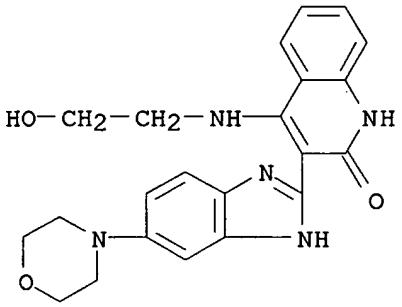
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO2H, certain NH2 derivs.; R1-R4 = H, halo, cyano, NO2, OH or derivs., NH2 or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO2H and esters and amides; R5-R8 = H, halo, NO2, OH or derivs., NH2 or derivs., SH or derivs., cyano, etc.; R9 = H, OH, (un)substituted alkoxy or aryloxy, NH2 or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH2 or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R1-R8 = H, halo, NO2, cyano, OH or derivs., NH2 or derivs., acyl, SH or derivs., etc.; R9 = H, OH, (un)substituted alkoxy, aryloxy, NH2 or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prepared by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed prepns. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (prepns. given), carried out in refluxing ClCH2CH2Cl in the presence of SnCl4, gave the invention quinolinone III. Many compds. I and II had in vitro IC50 values of less than 10 μM with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

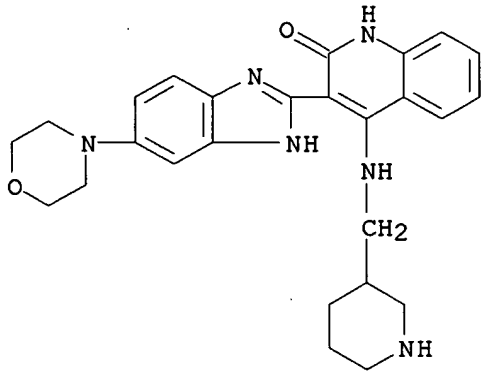
IT 405168-26-5P 405168-29-8P 405168-30-1P
405168-31-2P 405168-32-3P 405168-34-5P,
4-[((2S)-2-Amino-4-methylpentyl)amino]-3-[5-(morpholin-4-yl)benzimidazol-2-

yl]-1H-quinolin-2-one 405168-35-6P, 4-[((2S)-2-Amino-3-methylbutyl)amino]-3-[5-(morpholin-4-yl)benzimidazol-2-yl]-1H-quinolin-2-one 405168-38-9P 405168-39-0P 405168-40-3P 405168-41-4P 405168-47-0P 405170-04-9P, 3-(1H-Benzimidazol-2-yl)-4-(dimethylamino)quinolin-2(1H)-one 405170-84-5P, 3-(1H-Benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]-2(1H)-quinolinone 405170-85-6P 405170-86-7P, 4-[(2-Amino-4-methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone 405170-87-8P , 4-[(2-Amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

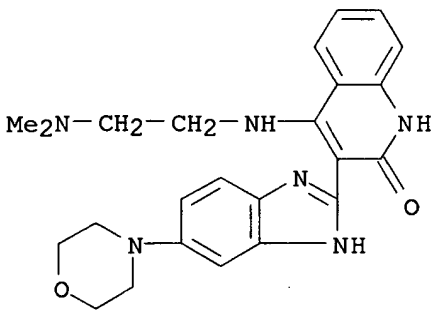
RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



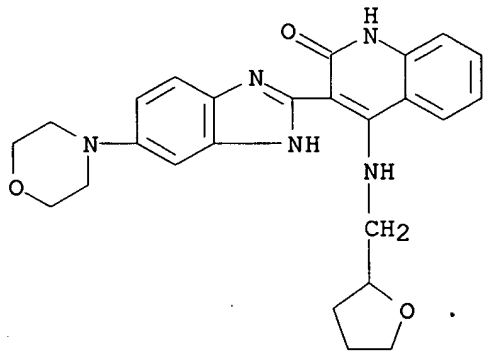
RN 405168-29-8 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



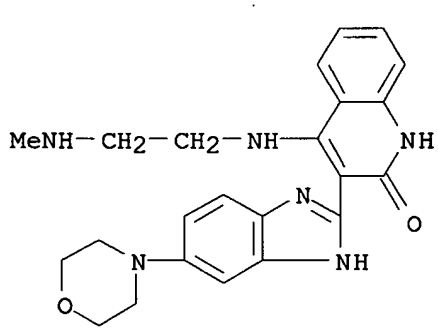
RN 405168-30-1 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(dimethylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



RN 405168-31-2 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

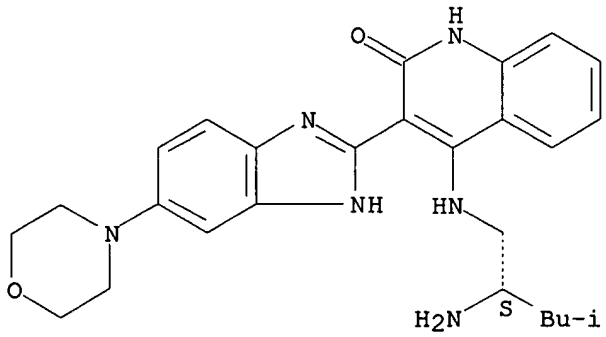


RN 405168-32-3 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(methylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



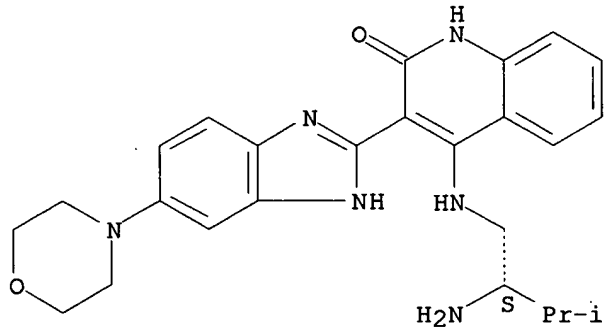
RN 405168-34-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[[(2S)-2-amino-4-methylpentyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

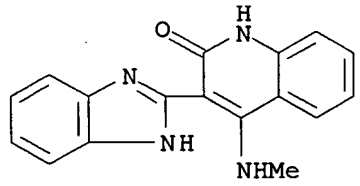


RN 405168-35-6 CAPLUS
CN 2(1H)-Quinolinone, 4-[[(2S)-2-amino-3-methylbutyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

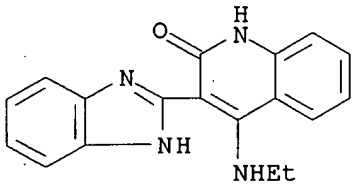
Absolute stereochemistry.



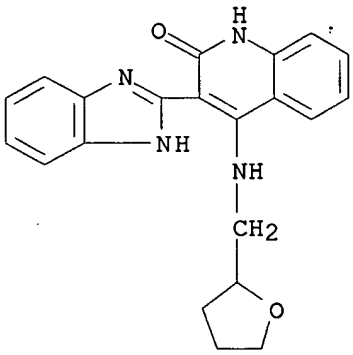
RN 405168-38-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(methylamino)- (9CI) (CA INDEX NAME)



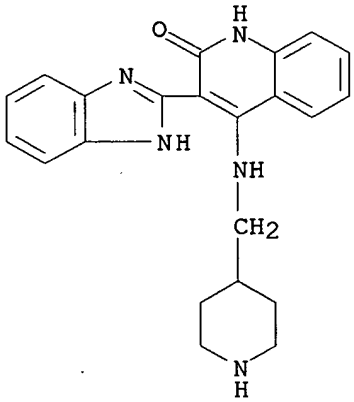
RN 405168-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(ethylamino)- (9CI) (CA INDEX NAME)



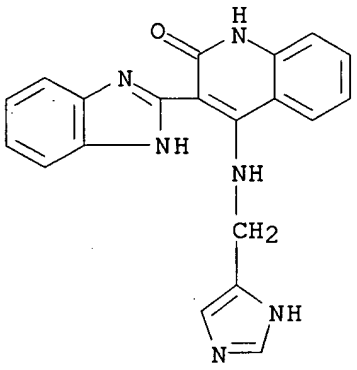
RN 405168-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 405168-41-4 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 405168-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-4-ylmethyl)amino]- (9CI) (CA INDEX NAME)



RN 405170-04-9 CAPLUS
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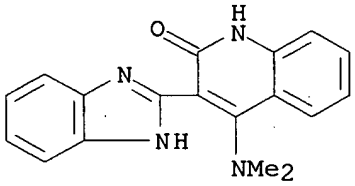
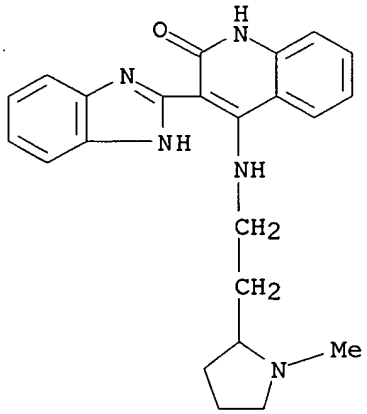
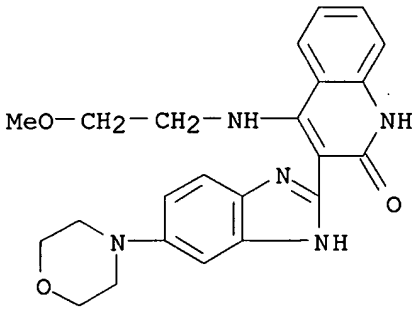


RN 405170-84-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 405170-85-6 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



RN 405170-86-7 CAPLUS
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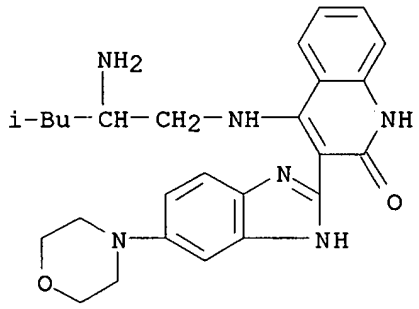
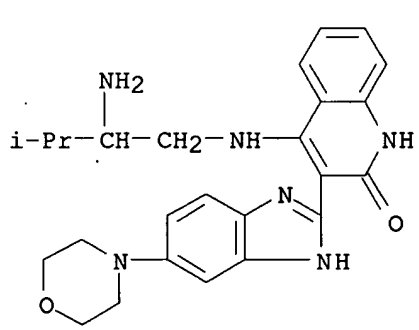
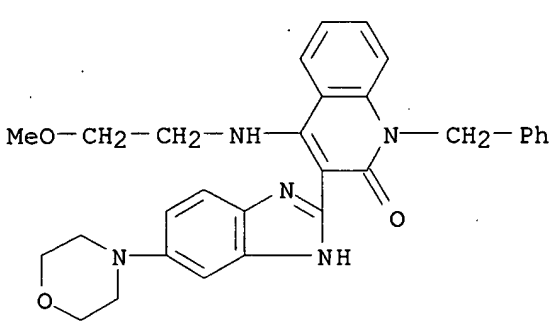


RN 405170-87-8 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



IT 405171-07-5P, 4-[(2-Methoxyethyl)amino]-3-[5-(morpholin-4-yl)benzimidazol-2-yl]-1-benzyl-1H-quinolin-2-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)
RN 405171-07-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-

benzimidazol-2-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:220574 CAPLUS
DN 136:263158
TI Benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents
IN Renhowe, Paul; Pecchi, Sabina; Machajewski, Tim; Shafer, Cynthia; Taylor, Clarke; McCrea, Bill; McBride, Chris; Jazan, Elisa; Wernette-Hammond, Mary-Ellen; Harris, Alex
PA Chiron Corporation, USA
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002022598	A1	20020321	WO 2001-US42131	20010911
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	NZ 524717	A	20040924	NZ 2001-524717	20010911
	AT 309996	E	20051215	AT 2001-973722	20010911
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	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
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	US 2005054672	A1	20050310	US 2004-886950	20040708
	US 2005209456	A1	20050922	US 2005-92137	20050329
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	US 2002-284017	A1	20021030		
	US 2004-886950	A1	20040708		
OS	MARPAT 136:263158				
GI					

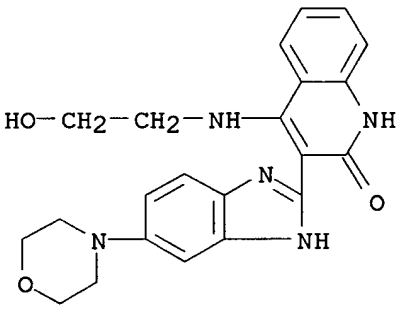
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO2H, certain NH2 derivs.; R1-R4 = H, halo, cyano, NO2, OH or derivs., NH2 or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO2H and esters and amides; R5-R8 = H, halo, NO2, OH or derivs., NH2 or derivs., SH or derivs., cyano, etc.; R9 = H, OH, (un)substituted alkoxy or aryloxy, NH2 or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH2 or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R1-R8 = H, halo, NO2, cyano, OH or derivs., NH2 or derivs., acyl, SH or derivs., etc.; R9 = H, OH, (un)substituted alkoxy, aryloxy, NH2 or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prepared by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed prepns. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (prepns. given), carried out in refluxing ClCH2CH2Cl in the presence of SnCl4, gave the invention quinolinone III. Many compds. I and II had in vitro IC50 values of less than 10 μM with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

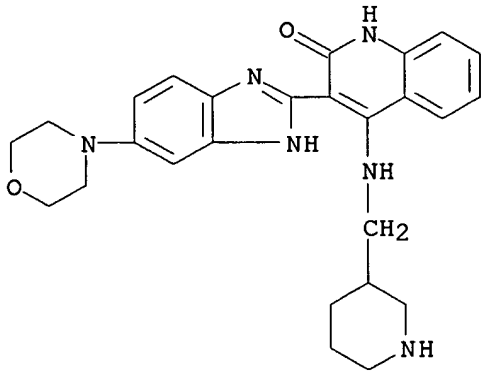
IT 405168-26-5P 405168-29-8P 405168-30-1P

405168-31-2P 405168-32-3P 405168-34-5P,
4-[((2S)-2-Amino-4-methylpentyl)amino]-3-[5-(morpholin-4-yl)benzimidazol-2-yl]-1H-quinolin-2-one 405168-35-6P, 4-[((2S)-2-Amino-3-methylbutyl)amino]-3-[5-(morpholin-4-yl)benzimidazol-2-yl]-1H-quinolin-2-one 405168-38-9P 405168-39-0P 405168-40-3P
405168-41-4P 405168-47-0P 405170-04-9P,
3-(1H-Benzimidazol-2-yl)-4-(dimethylamino)quinolin-2(1H)-one
405170-84-5P, 3-(1H-Benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]-2(1H)-quinolinone 405170-85-6P
405170-86-7P, 4-[(2-Amino-4-methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone 405170-87-8P
, 4-[(2-Amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)

RN 405168-26-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

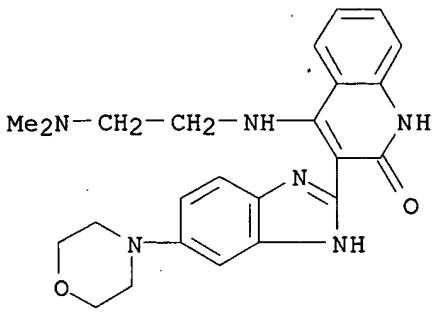


RN 405168-29-8 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(3-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

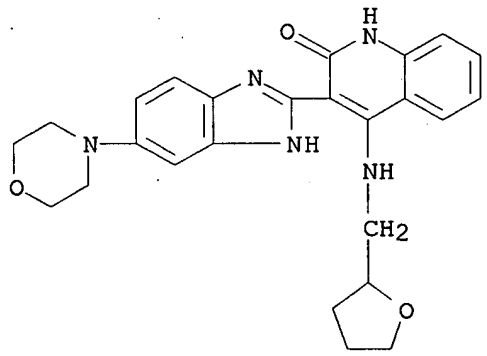


RN 405168-30-1 CAPLUS

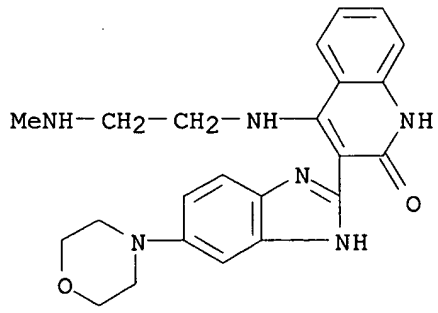
CN 2(1H)-Quinolinone, 4-[[2-(dimethylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



RN 405168-31-2 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

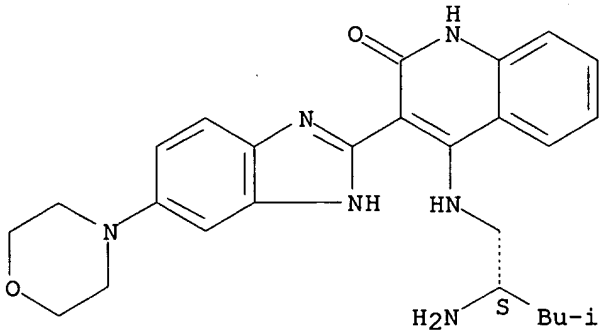


RN 405168-32-3 CAPLUS
CN 2(1H)-Quinolinone, 4-[[2-(methylamino)ethyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



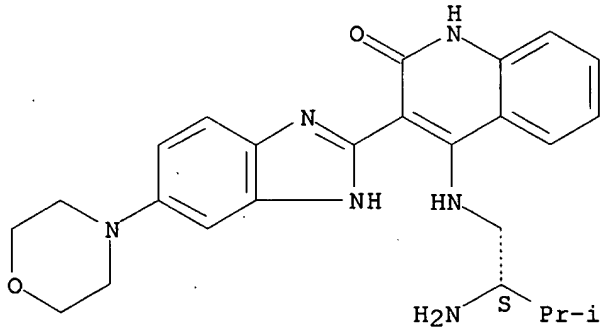
RN 405168-34-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[[(2S)-2-amino-4-methylpentyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

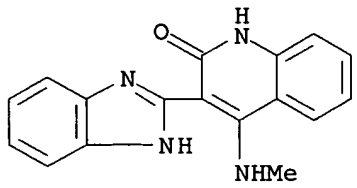


RN 405168-35-6 CAPLUS
CN 2(1H)-Quinolinone, 4-[[(2S)-2-amino-3-methylbutyl]amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

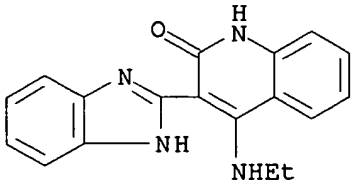
Absolute stereochemistry.



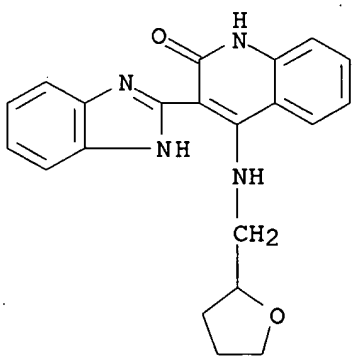
RN 405168-38-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(methylamino)- (9CI) (CA INDEX NAME)



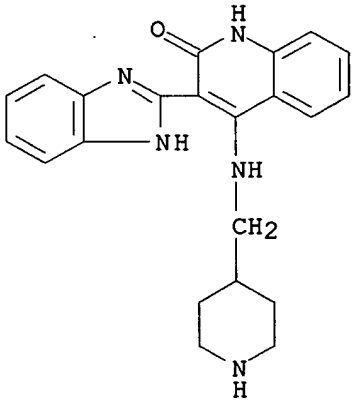
RN 405168-39-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(ethylamino)- (9CI) (CA INDEX NAME)



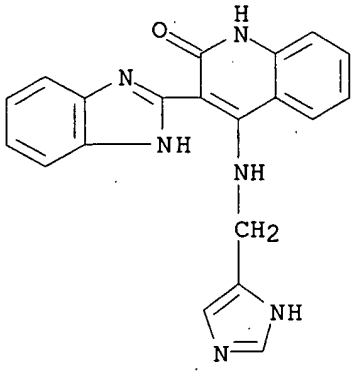
RN 405168-40-3 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



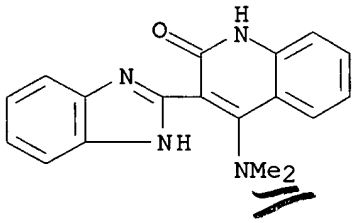
RN 405168-41-4 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(4-piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)



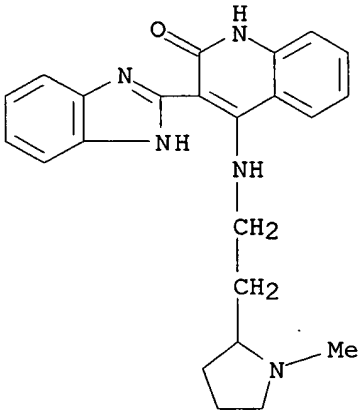
RN 405168-47-0 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-4-ylmethyl)amino]- (9CI) (CA INDEX NAME)



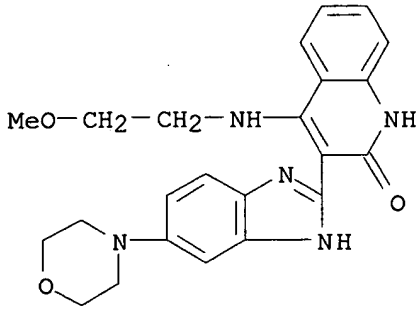
RN 405170-04-9 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)- (9CI) (CA INDEX NAME)



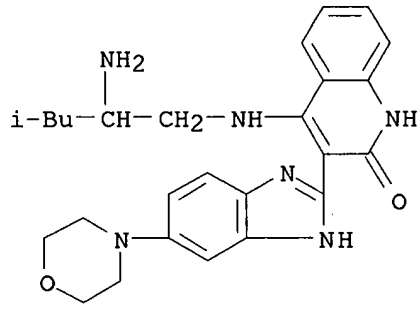
RN 405170-84-5 CAPLUS
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



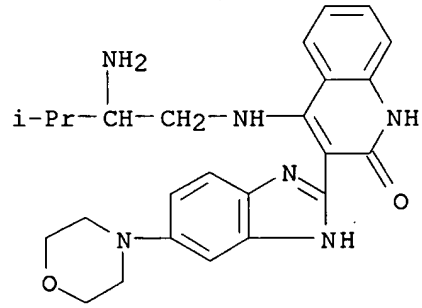
RN 405170-85-6 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



RN 405170-86-7 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-4-methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)

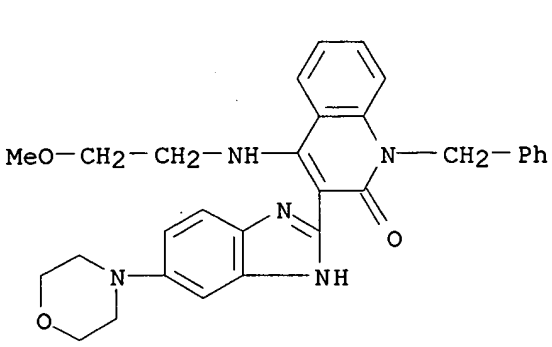


RN 405170-87-8 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



IT 405171-07-5P, 4-[(2-Methoxyethyl)amino]-3-[5-(morpholin-4-yl)benzimidazol-2-yl]-1-benzyl-1H-quinolin-2-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzimidazolyl-substituted quinolinone derivs. and analogs as VEGFR tyrosine kinase-inhibiting anticancer agents)
RN 405171-07-5 CAPLUS
CN 2(1H)-Quinolinone, 4-[(2-methoxyethyl)amino]-3-[5-(4-morpholinyl)-1H-

benzimidazol-2-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



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L3 STRUCTURE UPLOADED

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